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HISTIOCYTIC RETICULOSIS IN INFANTS.

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AN examination of the literature in relation to the reticulo-endothelioses reveals that many pathological conditions have been included under this general heading, and much confusion exists, not a little of which is due to the variety of names that have been used. Four of these conditions appear to have a particular bearing upon the cases about to be discussed; these are (*a*) Letterer-Siwe's disease, (*b*) eosinophilic granuloma of bone, (*c*) infective reticulo-endotheliosis and (*d*) Hand-Schüller-Christian disease.

Letterer-Siwe's Disease.

The title Letterer-Siwe's disease was first used, or more correctly was coined, by Abt and Denenholz[1] in 1936. These authors explain that, in an endeavour to identify a case which had come under their notice, they made a review of the literature, and found that a case very similar to their own was first reported by Letterer in 1924. They go on to state that Siwe reported another case in 1933, and that he analysed the case reported by Letterer and two others which had been reported meanwhile, one by Akiba and the other by Guizetti.

Some difference of opinion seems to exist, however, as to which cases were reported first, since Foot and Olcott[2] state that "authorities are apparently agreed that the first cases to be published were those of Borissowa". Nevertheless the term Letterer-Siwe's disease has obtained some degree of recognition during the short time that it has been in use.

Robb-Smith[3] makes brief mention of this condition under the heading of reticulum-celled medullary reticulosis, which he identifies with Letterer-Siwe's disease, and which, he states, has also been described by Oberling and Guerin as the acute reticulosis of infants. Robb-Smith states that a similar disease occurs in adults, with a clinical picture resembling that of typhoid fever or "a generalized lymphadenopathy, frequently fatal within a year".

Hadfield and Garrod[4] also refer to an acute reticulosis which occurs in infants of the average age of sixteen months; to this condition they give the name primary medullary reticulosis. These authors agree with Robb-Smith[3] that "a few cases of a similar disease have been described in adults, but the course is usually longer".

Siwe, as quoted by Abt and Denenholz,[1] has stated that this disease occurs exclusively in infants and is neither of an hereditary nor of a familial character. The usually accepted clinical picture is one of generalized lymph node enlargement and splenomegaly with an hæmorrhagic tendency, and the presence of a skin eruption which is persistently referred to as either petechial or hæmorrhagic. There is no characteristic blood picture, and in the current conception the histopathology consists of a generalized hyperplasia of non-lipoid-storing macrophages occurring to a varying extent throughout the reticulo-endothelial system. In the tissues and organs involved, the normal architecture has been found to be distorted, while areas of hæmorrhage and necrosis have been frequently noted in the cellular aggregates.

Eosinophilic Granuloma of Bone.

The term eosinophilic granuloma of bone was originally used by Lichtenstein and Jaffe[5] in their report of the case of a four-year-old girl who had a solitary lesion of the left femur. This lesion, which in skiagrams appeared as a fusiform area of rarefaction, was opened surgically and the soft tissue removed by curettage. This tissue was highly cellular and was found to consist of sheet-like masses of large cells, which the authors described as either wandering macrophages or histiocytes derived from

the reticulum cells of the part. A striking feature was the presence, in the lesion, of abundant eosinophile leucocytes; multinucleated giant cells and occasional lymphocytes, plasma cells and neutrophile leucocytes completed the picture.

In this, their first paper on the subject, Lichtenstein and Jaffe[6] described eosinophilic granuloma of bone as a well-defined, localized, single lesion starting in the medullary cavity and tending to erode, expand and perforate the cortex. In a search of the literature they recognized only four cases previously reported which they believed corresponded with the entity which they had described. Quite independently and almost simultaneously, Otani and Ehrlich[9] published a report of four cases under the title of "solitary granuloma of bone, simulating primary neoplasm". Later these authors agreed, as stated by Lichtenstein and Jaffe,[5] that the cases they had reported could be classified as examples of eosinophilic granuloma of bone.

An added understanding of this subject resulted from the publication by Green and Farber[7] of ten cases of eosinophilic granuloma of bone, which they had collected over a period of twelve years. The various clinical manifestations of the disease were dealt with in this paper, and it was pointed out that the lesions in bone in these cases were not always solitary, but that multiple lesions could occur, and in six of their reported cases multiple lesions were present, all of which were located in bone.

The descriptions of the histological appearances in the biopsy material taken from such cases and reported by various authors[3][9][10] do not differ in any essential from the original descriptions of Lichtenstein and Jaffe[6] and of Otani and Ehrlich,[9] though Green and Farber[7] described what they considered to be the histological progression of these lesions from early to late stages. The tissue is described as being highly vascular and liberally infiltrated with large, pale, mononuclear cells, eosinophile leucocytes and occasional giant cells; patches of hæmorrhage and necrosis are to be seen.

Infective Reticulo-Endotheliosis.

Infective reticulo-endotheliosis was the title used by Van Creveld and Ter Poorten[11] in an article describing a case of non-lipoid reticulo-endotheliosis. A study of this case report and of the many excellent photomicrographs which are included confirms the opinion expressed by these authors, that this condition is indistinguishable, at least on histo-pathological grounds, from those cases reported under the various titles which are accepted as being synonymous with Letterer-Siwe's disease.

Hand-Schüller-Christian Disease.

It is generally assumed that Hand-Schüller-Christian disease is essentially the same as those conditions reported under the titles lipoid histiocytosis and lipoid granulomatosis, so that it may be looked upon as a process of generalized reticulo-endothelial hyperplasia, in which bones, lungs, liver, spleen and lymph nodes may be involved, and in which the classical triad of *diabetes insipidus*, exophthalmos and defects in the membranous bones may be entirely absent. In this disease the feature which has been selected for attention is the foamy nature of the cytoplasm of the histiocytes, due to the presence of cholesterol fatty-acid esters. What are spoken of as xanthoma nodules may occur in the skin, and according to Ellis[12] there may also be less characteristic eczematous eruptions.

Glanzman[13] drew attention to the similarity in structure between the localized lesions found in the bones in Hand-Schüller-Christian disease and the widespread lesions of Letterer-Siwe's disease; while Wallgren[14] has presented evidence to suggest that the conditions mentioned are essentially similar. Farber[8] was the first to suggest that eosinophilic granuloma of bone might well be a condition allied to both Hand-Schüller-Christian disease and Letterer-Siwe's disease.

The Present Series.

In the material presented here it is intended to show that a basic pathological pattern is discernible in each case, and this type of tissue reaction, which is common to them all, is histiocytic granulation tissue. This term embraces a wide range of vascular and fibrocellular connective tissue, and presents the appearances of granulation tissue in various stages of maturity, but of a distinctive character, since it contains as part of its cellular content an appreciable number of large, pale and often multinucleated histiocytes. This term will be used frequently in the text to indicate a special type of tissue response common to the conditions about to be described, and basic to an understanding of their allied character.

CASE I.—Case I of this series is an example of Letterer-Siwe's disease. The patient, a female infant, died at the age of fifteen months, after an illness which lasted seven weeks. The illness was characterized by a rapid and enormous enlargement of the mediastinal and cervical lymph nodes; enlarged, though smaller, lymph nodes were present in the axillary and inguinal regions. Three days before death a fine red rash appeared upon the trunk.

At autopsy the skin of the trunk felt finely granular, owing to the presence there of closely set, small, red elevations of the epidermis. The cut surface of the enlarged lymph nodes was moist and pink; small areas of hæmorrhage and necrosis were present in the larger examples. In the region usually occupied by the thymus was material partly necrotic and partly fibrous, and many gritty, calcified particles were present in the necrotic parts. The pericardium, the visceral pleura and the connective tissue septa of the lungs were all increased in thickness, and the pancreas was bound in tough fibrous tissue.

The accompanying photomicrographs have been chosen to depict the two essential features of the pathology in this case. Figure I was taken from one of the enlarged cervical lymph nodes, and it shows that the lymphoid tissue was replaced to a large extent by histiocytes. A small number of lymphocytes remained, and in addition there were very occasional polymorphonuclear neutrophile and eosinophile leucocytes. In Figure II the characteristic appearance of the histiocytes is more clearly shown, and although this figure contains only mononuclear forms, occasional cells of this type contained two or more nuclei.

Changes essentially similar to those found in the lymph nodes were present in the spleen, where histiocytes were arranged in large clusters; the centres of these clusters were often necrotic. In the liver focal collections of histiocytes had pushed aside the liver columns, while in the bone marrow histiocytes occurred singly, or in groups of two or three.

Figures III, IV, V and VI show various stages in the development of histiocytic granulation tissue. Figure III represents an early stage in the development of this tissue, and was taken from one of the thickened septa in the lung. Vascular channels are not easily recognizable in this figure, but young connective tissue cells and histiocytes, one of which is multinucleated, can be clearly seen. In addition there were present in this part many polymorphonuclear leucocytes, lymphocytes and occasional eosinophile leucocytes. Figure IV is taken from a portion of the thickened visceral pleura and shows the fibroblastic nature of the histiocytic granulation tissue in this situation. In the deeper parts, adjacent to the pulmonary alveoli, the fibroblasts are arranged parallel to the surface, but in the superficial parts they assume a more perpendicular arrangement. Histiocytes are present in small numbers, but they are easier to define in Figure V, which shows a portion of the same tissue more highly magnified. The cicatricial stage of histiocytic granulation tissue is shown in Figure VI, in tissue taken from the parietal pericardium. Very few histiocytes were found in this older form, and a few of those which were present had a foamy cytoplasm. The tissue which surrounded and invaded the pancreas was histiocytic granulation tissue, and similar tissue was found between the periosteum and the bone of one of the ribs.

CASE II.—Case II could be classed as an example of eosinophilic granuloma of bone. The patient was a male infant, who presented at the age of sixteen months with bilateral swellings of the mastoids. At exploratory operation it was found that the bone in these parts was thinned and in some parts eroded by a soft vascular tissue. Portion of this tissue was curetted out, and histological examination revealed that it was histiocytic granulation tissue liberally infiltrated with eosinophile cells. Portion of this tissue is shown in Figure VII, and in this the darkly staining

cells, which represent the eosinophile leucocytes, are so numerous that the larger, pale histiocytes tend to be obscured.

Three days after the operation the spleen became enlarged and at the same time a petechial rash appeared upon the trunk. One week later the cervical lymph nodes became greatly enlarged, and this enlargement was closely followed by an enlargement of the axillary and inguinal lymph nodes. Figure VIII is taken from one of the inguinal lymph nodes which was removed soon after it became enlarged. This figure reveals that at this time the lymphoid tissue of the node had been completely replaced by histiocytes and eosinophile leucocytes; the majority of the histiocytes in this part are multinucleated.

The condition of the patient gradually deteriorated, and he died eight months after the onset of the illness from bilateral lobar pneumonia.

At autopsy some of the small epidermal elevations on the trunk were red, while others had taken on a brownish tint. Upon histological examination these papules were found to be caused by collections of histiocytes in the outer layers of the dermis (see Figure IX). Lymphocytes, occasional eosinophile leucocytes and red cells were also present, and the lesion did not differ in any essential from the skin lesions examined in Case I.

There was a circular defect of the right occipital bone; this is shown in Figure X. Figure XI shows the radiographic appearance of a bony lesion found in the distal third of the left femur (taken from autopsy specimen). The bony trabeculæ were destroyed in this part and replaced by a tissue which in some parts was soft and gelatinous and in others tough and fibrous. This was composed of histiocytic granulation tissue in various stages of development; no eosinophile leucocytes were present. A similar lesion was present in the neck of the right femur.

The lymph nodes in the neck were fibrous. Some of the histiocytes in this part contained hæmosiderin granules, others were foamy. In the lymph nodes elsewhere the lymphoid tissue was partly or wholly replaced by histiocytes; no eosinophile cells accompanied these lesions.

CASE III.—Case III could be classified as Hand-Schüller-Christian disease. The patient was a male infant who died at the age of fifteen months. He was thought to have been quite well until three months previously, at which time he developed a cough which had persisted.

At autopsy there was a fine, raised, red rash upon the trunk similar to that described in Cases I and II. A circular defect in the right occipital bone was enclosed by fibrous tissue, while between these fibrous layers histiocytic granulation tissue was found upon histological examination. Many of the histiocytes in this part were multinucleated, and the majority had a foamy cytoplasm; in frozen sections these stained brightly red with *Scharlach R.* Small clusters of eosinophile leucocytes were also present, together with lymphocytes and plasma cells.

The lungs were tough to cut and almost airless, and this was due to a marked increase in the interstitial fibrous tissue in which histiocytes and lymphocytes were very numerous; there were no foam cells in this part.

Examination of the lymph nodes, which were moderately enlarged, revealed perivascular accumulations of histiocytes.

CASE IV.—Case IV of the series reveals a mixed picture of lipoid and non-lipoid histiocytosis without any localized lesion in bone. The patient was a female infant, aged thirteen months, who for three months had been suffering from progressive loss of weight and associated abdominal distension. Three weeks before her death the spleen and lymph nodes became enlarged and a red rash appeared upon the trunk.

At autopsy the rash was found to be, in all essentials, similar to the epidermal lesions present in Cases I, II and III. A yellow, gelatinous material was present upon the inner surface of the dura, upon either side of the mid-line. Similar tissue had caused an increase in thickness of the walls of the cavernous sinuses, and this had come to surround the stalk of the pituitary. The cells composing this material were largely histiocytes, some of which were multinucleated, and many had a foamy cytoplasm. Figure XII shows the general arrangement of this tissue, and Figure XIII, in which the same cells are more highly magnified, reveals that many of the histiocytes may be classed as foam cells. An abundance of lipoid-laden histiocytes, all of which stained brightly with *Scharlach R,* were present in a mottled zone of red and yellow which surrounded the pelvis of each kidney.

The enlarged lymph nodes and spleen were packed with histiocytes, none of which were foamy, while the adrenal glands, pancreas and thyreoid gland were surrounded by a thick layer of histiocytic granulation tissue. Figure XIV is an example of early histiocytic granulation tissue which was present in the visceral pleura. The interlobular septa, in all parts of the lung examined, were increased in thickness by a similar tissue, and such tissue was present also in the alveolar walls.

Discussion.

Since no ætiological factor has been determined in any of the conditions mentioned in the introduction, any attempt at classification must be made upon the basis of similarities and differences in the morphology of the lesions disclosed. It is upon this basis that the conditions reported as infective reticulo-endotheliosis, acute reticulosis of infants, non-lipoid histiocytosis, and reticulum-celled medullary reticulosis are assumed to be identical.

When an attempt was made to classify Case I in this manner no particular difficulty was encountered. A comparison of the pathological changes in this case with the criteria given by Siwe, and a close study of the cases reported by Abt and Denenholz,[1] by Foot and Olcott,[2] and by Gross and Jacox,[10] left no doubt that this was the type of case reported under the title of Letterer-Siwe's disease, or its various synonyms—and this despite the fact that in the case here reported a specific granulation tissue was an essential and distinctive feature of the pathology. Case II, however, was more difficult to classify. The illness began with localized swellings of the bones of the skull, and the material obtained from these regions at biopsy presented a histological picture in every way identical with that obtained from cases reported as of eosinophilic granuloma of bone. Although the local lesions healed after a radical operation, the disease did not remain localized, but in fact became generalized. That this generalization was due to the same disease process that attacked the bones of the skull was evident by the involvement, at this time, of the inguinal lymph nodes, to produce a pathological picture, as proved by biopsy, in which histiocytes and eosinophile leucocytes predominated. At this stage it would have been reasonable to assume that this case was an example of eosinophilic granuloma of bone, which, instead of remaining localized, as usually happens in this disease, had become generalized. This assumption would be supported by the statement of Gross and Jacox[10] that a case of eosinophilic granuloma of bone has been described in which there was involvement of the regional lymph nodes. At autopsy, however, the massive eosinophilic infiltration, so characteristic of the biopsy material, had largely disappeared, and comparison of the histo-pathological findings in the autopsy material with that obtained from Case I, showed so many features in common that any segregation of these two cases into two distinct categories was unwarranted.

Since the presenting sign in Case III was a localized skull defect occupied by tissue which proved to be lipoid granulation tissue, it seemed reasonable to suggest that this case might represent an example of Hand-Schüller-Christian disease. This tissue, however, contained clusters of eosinophile leucocytes, and not all of the histiocytes were foamy. In view of the experience obtained from the study of Case II, the decision seemed to rest between Hand-Schüller-Christian disease and eosinophilic granuloma of bone. When the other organs from this patient were examined, many were found to be infiltrated by histiocytes or involved by histiocytic granulation tissue. These affected areas contained only an occasional eosinophile leucocyte, and the histiocytes were not foamy. Indeed, it became apparent that, apart from the lesion in the skull and a difference in the degree of involvement of the tissues in this case, the pathological changes did not differ sufficiently from those of Case I to allow of a separate classification.

Case IV presented none of the classical triad of Hand-Schüller-Christian disease; yet many of the histiocytes were lipoid-laden, or formed areas of lipoid granulation tissue, and to judge from the position of the lipoid granulation tissue enclosing the stalk of the pituitary, some evidence of hypothalamic dysfunction might have occurred. These lipoidal areas, however, contributed only in a small

degree to the pathology of this case, and apart from them no clear line of demarcation existed between this case and Case I.

It was clear that it was not reasonable, upon purely morphological grounds, to separate these cases into a series of distinct entities. That such a separation has existed is not surprising, for there is little similarity clinically in the varying expressions of this disease. Even in the cases recorded here, in all of which the subjects were infants under the age of two years, and in which the disease progressed fairly rapidly to death, there is little beyond the skin rash which would serve to link these cases as one entity in the mind of the clinical observer. This lack of clinical similarity is even more obvious when cases are considered from a wider age group, as this would include the so-called typical cases of eosinophilic granuloma of bone and of Hand-Schüller-Christian disease.

As was previously noted, suggestions have been put forward that these conditions are related. Even so, undue attention has been focused on two types of cells, the eosinophile leucocytes and the foam cells—cells which are of little significance as they affect classification, though their presence poses interesting questions which are so far not completely answered. While attention has been focused on these elements, the basic structure of the lesion, the histiocytic granulation tissue, has not been stressed sufficiently. Careful studies have been made on the natural progression of the lesion in bone, in the case of eosinophilic granuloma of bone, by Green and Farber,[7] who showed that there were an increasing fibrosis and decreasing cellularity as the lesion aged. The eosinophile cells disappeared and the histiocytes became converted into foam cells. Jaffe and Lichtenstein,[15] while not doubting this sequence of events, pointed out that in a case observed by them there was no absolute evidence that such a progression occurred; the lesion resolved, leaving little or no trace; there was no residual fibrosis and no foam cells were found. There is nothing mutually contradictory in this, and it is what might be expected to occur in any inflammatory disease. There is ample reason to believe, on pathological evidence, that these allied or identical conditions are inflammatory, even though there is, as yet, no knowledge of the inflammatory agent. Despite what has just been said, the current conception of Letterer-Siwe's disease would still appear to be one in which there is a proliferation of the histiocytes in many organs and tissues, a concept expressed in the term aleuchæmic reticulosis. Others, however, accept the idea that healing may occur in some lesions, when the condition is said to merge into Hand-Schüller-Christian disease. If the inflammatory nature of this disease (histiocytic reticulosis) is accepted, then, it is true, cases may occur which are so acute and in which the course is so rapid that the entire pathological process will be exudative in nature. However, on the basis of the material examined from Case I, there is some reason to doubt this. In that instance the disease was unquestionably acute and rapidly fatal, though death occurred in a matter of weeks and not days. Even in such a rapidly progressive case as this, two types of inflammatory reaction were found developing concurrently. One was entirely cellular and the histiocytes presented as practically unsupported cellular aggregations. This has been termed the exudative type of reaction, whilst it is realized that many of these cells must have proliferated locally. This type of reaction was found predominantly in cellular tissues, such as lymph nodes, bone marrow and spleen. Necrosis had occurred in these cellular aggregates, but there was no evidence of any progressive tissue reaction. The other type of reaction was proliferative, and, as far as could be judged, it was proliferative from the onset. This type of reaction occurred in connective tissue and produced the characteristic histiocytic granulation tissue. The mode of progression of this tissue has been traced in the text through all the stages of early, fibroblastic and cicatricial granulation tissue. It is to be noted, however, that in this case there was no concurrent transformation of histiocytes to foam cells; rather was there evidence to point to the transformation of many of the histiocytes to fibroblasts and the formation of a dense fibrous scar, in which, perhaps, an occasional foam cell might be found. It does not seem necessary, in the case of Letterer-Siwe's disease, to recognize the transformation of early lesions to later lipo-granulomatous lesions, to understand the close relationship which exists between this condition and Hand-Schüller-Christian disease. Similarly, it is unnecessary to find abundant eosinophile cells in lesions from Letterer-Siwe's disease, in order to recognize that eosinophilic granuloma of bone and Letterer-Siwe's disease are merely varying manifestations of the same disease. What is necessary is to identify the underlying pathology of all these reactions, which have their common ground in the formation of histiocytic granulation tissue. The fact, as exemplified by Case II of this series, that eosinophile cells are not limited to the lesions which occur in bone, does help, however, to establish the idea that Letterer-Siwe's disease and eosinophilic granuloma of bone are identical. Jaffe and Lichtenstein,[15] reporting a case rather similar to Case II of this series, refer to their case as an example of Letterer-Siwe's disease, but with the addition of a lesion in bone identical with eosinophilic granuloma of bone. Their use of this somewhat confused terminology would seem to result from their belief that it is only in destructive lesions of bone that large numbers of eosinophile cells occur. Such a view can no longer be substantiated on the evidence obtained in Case II. The lymph node, which was removed in this case at a site distant from the lesions which were present in bone, contained eosinophile cells in abundance, and it would not be unreasonable to assume that many, if not all, of the organs and tissues which were affected at this time would have shown a similar picture. A small number of eosinophile cells were found in many of the lesions in Case I, and it is not unlikely that the very early lesions of Letterer-Siwe's disease may show these cells in greater profusion. Early lymph node biopsy in such cases should serve to clarify this point. The belief that eosinophile cells are present in large numbers only in the early stages is supported by this study; but they would appear to persist longer in the skeletal lesions than elsewhere. They have been reported frequently in the bone lesions of Hand-Schüller-Christian disease, and they were present in appreciable numbers in the skull in Case III, though they were not present elsewhere in that case. Cases III and IV serve to confirm the idea expressed above, that all the lesions in this disease, histiocytic reticulosis, do not pass through a regular sequence of which foam cell formation is a part. That completely fibrous lesions may not contain foam cells is not surprising, for that is an end result and the lesion is then entirely healed; but in Cases III and IV all stages of progression could be studied, and though some lesions contained lipoid-laden cells, the majority did not. It does not appear to be possible to recognize any stage in the progression of these lesions in which foam cells may with certainty be expected to be found.

As a result of the work of Rowland,[16] Hand-Schüller-Christian disease was universally accepted as belonging to the group of lipoid storage diseases, and this despite the fact that Hand-Schüller-Christian disease had not been shown to be hereditary, and had, unlike any of the true lipoid storage diseases, a background of granulation tissue. Such a granulomatous lesion does not result from the storage of cholesterol in those instances in which the blood level of this substance is elevated. It is evident that the foamy lesions resulting from cholesterol storage, and those which sometimes result from the onward progression of histiocytic granulation tissue, have not been adequately differentiated in the past. As a result of this, confusion still results from the descriptions which remain current in most standard works, since these leave the impression that Hand-Schüller-Christian disease can be distinguished from other lipoid storage conditions only by the type of lipoid present in the cells.

Even with the newer knowledge of the close relationship which exists between the seemingly distinct diseases mentioned in this text, confusion will remain until some uniform nomenclature is adopted. It may be preferable, but it hardly seems necessary, to wait until a common ætiological agent is discovered before a classification is attempted. Mallory[17] has put forward certain suggestions relating to this question, and these may well be considered

as a working basis. The following arrangement is suggested as an attempt at a usable classification: Histiocytic reticulosis (inflammatory): (i) acute, to include all cases of Letterer-Siwe's disease, and those instances of eosinophilic granuloma of bone which are rapidly progressive; (ii) subacute, to include eosinophilic granuloma of bone, with single or multiple lesions of bone, and with or without visceral lesions, some of which may eventually be lipogranulomata; (iii) chronic, to include slowly progressing histiocytic or lipo-granulomatous lesions of bone or of viscera, or of both, and also certain fibrous lesions in which the underlying pathology can be identified. The majority of the cases of Hand-Schüller-Christian disease would fall into this group.

Summary.

Four cases have been described which represent varying manifestations of one disease, histiocytic reticulosis, a disease which is probably inflammatory in origin. Emphasis has been placed on a unifying pathological reaction which occurs in these cases, notably histiocytic granulation tissue. This tissue may undergo many alterations during its life history, and, moreover, it is subject to certain variations. The reasons why such variations should occur are, to say the least, imperfectly understood.

A plea is made for the adoption of some uniform nomenclature which will embrace all these conditions and their multiple modes of presentation.

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Legends to Illustrations.

FIGURE I.—Cervical lymph node. The lymphoid tissue is largely replaced by histiocytes; the small, rounded, darkly staining bodies are the nuclei of lymphocytes. (× 200.)

FIGURE II.—Portion of cervical lymph node under higher magnification; histiocytes and lymphocytes are recognizable. (× 400.)

FIGURE III.—Early histiocytic granulation tissue from the connective tissue septa in the lungs. (× 400.)

FIGURE IV.—The fibroblastic stage of histiocytic granulation tissue from the thickened pleura. (× 200.)

FIGURE V.—Portion of Figure IV (× 400). The histiocytes are present, but in smaller numbers than in the earlier stage shown in Figure IV.

FIGURE VI.—The cicatricial stage of histiocytic granulation tissue (from the pericardium). Occasional histiocytes are visible. (× 200.)

FIGURE VII.—Histiocytic granulation tissue as seen in the biopsy material obtained from the left mastoid region. (× 200.)

FIGURE VIII.—A portion of the left inguinal lymph node removed at biopsy; the lymphoid tissue is replaced by mononuclear and multinuclear histiocytes and eosinophile leucocytes. (× 400.)

FIGURE IX.—One of the skin lesions. Widely spaced histiocytes and less numerous lymphocytes are present beneath the epidermis. Keratin is increased. (× 200.)

FIGURE X.—A portion of the occipital bone. The almost circular defect in the bone is closed by a thin membrane.

FIGURE XI.—Radiographic appearance of the lesion in the left femur.

FIGURE XII.—The cellular layer upon the inner surface of the *dura mater*. (× 200.)

FIGURE XIII.—A portion of Figure XII (× 400). The foamy nature of the majority of the histiocytes is evident.

FIGURE XIV.—Early histiocytic granulation tissue in the visceral pleura. (× 200.)

ALLERGIC DISEASES AND THE NOSE.[1]

By CHARLES SUTHERLAND,
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THE allergic diseases may, in a broad sense, turn out to be due to inability of a proportion of the race to adapt themselves to changes of environment. The human race has existed for perhaps 500,000 years and has evolved from lower forms of life for perhaps one hundred times that period, and during the whole of that vast stretch of time the environment has, we are told, changed only slowly. By contrast our present environment has changed rapidly and drastically, so that even our grandparents lived in a very different world.

Primitive man generally lived in Arcadian surroundings, in which there was a balance between forests, pasture and animals; dwellings were small and simple; food was scarce and "natural"; regular exercise was unavoidable and problems of immunity were simple. The small, isolated communities either adapted themselves to their own varieties of bacteria or they died out. Sharp axes, fire and the wheel have changed all that overnight (if we think in terms of geological time). Forests have been destroyed and replaced by vast tracts of pasture enriched by artificial fertilizers and protected by efficient fences; dwellings have become much larger and filled with complex furnishings gathered from all over the world or created by the chemists. We can eat all we want of novel foods, and we have no need to exert ourselves. Fast transport has provided unheard of opportunities for exchanging germs, so that an epidemic today in the remotest part of Asia may tomorrow menace Melbourne, whereas for our grandfathers it would have made interesting news months or years after it had subsided. Overcrowding in cities (trains, theatres and restaurants) provides novel means for exchange of bacteria, and upper

[1] Read at a meeting of the Ear, Nose and Throat Section of the Victorian Branch of the British Medical Association on November 17, 1947.

respiratory tract infections have become the curse of modern life for many. The contrast between Australia as Captain Cook found it and as it is today is striking, and it is small wonder that the respiratory tract especially suffers from these environmental changes. In a modern city the streets dry as soon as the rain stops, and gusty winds distribute a mixture of dusts wholesale. Organic ingredients such as pollen *et cetera* upset allergic subjects; but such dusts as the finely ground silica from the tram tracks probably cause a good deal of damage in all respiratory tracts.

Why some persons become allergic to certain organic dusts is still a mystery; but heredity is an important factor, and it is fairly certain that, when allergy is sufficiently severe to cause disease, it is because a normally useful mechanism is overacting.

Tobacco smoke appears to be harmful to some persons, although others live to a healthy old age in spite of liberal use of tobacco. It seems probable that the tarry products of smoking produce irreparable damage in some cases, and when asthma follows after years of excessive cigarette smoking, very little can be done. With all these mechanical, chemical and bacteriological assaults the real wonder is that there are so many relatively healthy noses.

When one is discussing environment, it is interesting to note that North America and Australia had (before Columbus and Captain Cook) sparse populations compared with other continents in the world. It is in these two continents that allergic diseases seem to be very prevalent. May this mean that these areas have some quality which is inimical to dense settlement? Both have at times dry atmospheres with turbulent winds. Living things are constantly adapting themselves to their surroundings, but there is a limit to their speed of adaptation. For this reason novelty is always dangerous to perfect health, and in the past century we have had much novelty in environment, in diet and in our sedentary mode of living.

THE ALLERGIC DISEASES.

The allergic diseases of chief interest to the rhinologist are seasonal hay fever, perennial hay fever (vasomotor rhinitis) and asthma. (Other important diseases in which allergy plays a part are atopic dermatitis and infantile eczema, contact dermatitis and urticaria.)

Hay Fever.

In Victoria seasonal hay fever due to grasses is prevalent from September to Christmas, is worse during hot north winds, is usually less severe at the seaside, and always disappears completely on the ocean or in the clean air of high mountains. Grass pollens produce strong reactions if applied to scratches on the skin, and desensitization generally produces satisfactory protection. But treatment by desensitization is tedious (twenty to thirty injections are required each season), it is moderately expensive, it is not always successful, and there is always a risk of constitutional reactions in unusually sensitive subjects. However, unless the pollens can be avoided, there appears to be no alternative, as other procedures such as zinc ionization, cauterization (chemical or thermal) and ultraviolet irradiation seem to be disappointing. In treatment one uses a set of dilutions of pollen extracts (1:1000, 1:100, 1:10 and full strength), and one commences by injecting a small dose of the 1:1000 solution. At each visit double the previous dose is injected until a dose is reached which produces a pronounced local reaction about half an hour after injection. This may be regarded as the first effective dose, and thereafter it is unsafe to give large increases; one must judge what dose to give by observing the effects of the previous injection. Usually one gives only 20% increases for the rest of the course. If insufficient caution is used, the patient will receive an overdose and develop shock, tachycardia, urticaria, œdema of the glottis or asthma and other unpleasant symptoms. Some subjects seem more prone to these constitutional upsets than others, and it is the risk of these upsets which makes treatment so tedious. A small group of patients have autumn hay fever, and these are found to be sensitive to the pollens of flowers such as the sunflower, dahlia, cosmos *et cetera*. For some reason the results of treatment of these are not so satisfactory.

The so-called "anti-histamine" drugs ("Benadryl", "Antistine" and "Anthisan") are useful in some cases of hay fever, but are generally disappointing in asthma. They are really excellent in severe urticaria. Many patients experience unpleasant side-effects from "Benadryl" (drowsiness, nausea and giddiness), and other drugs such as "Antistine" and "Anthisan" seem to be freer from such effects.

Perennial Hay Fever.

In perennial hay fever the allergen is present in the atmosphere throughout the year (house dust, feathers, kapok, animal danders, linseed, orris and silk *et cetera*) and therefore symptoms tend to be perennial also. In typical cases the patient reacts definitely to the allergen, and symptoms disappear if the allergen is removed or if the patient moves to a locality where the air is quite clean. This is really the "acid test"; if skin reactions are significant, avoidance of the allergen should produce prompt and complete relief. If it does not, either the reaction is not significant or there is some complicating factor.

Asthma.

The outstanding feature about asthma is the periodicity of symptoms. In many patients violent attacks of dyspnœa and wheezing alternate with periods of complete freedom from respiratory symptoms. Other fascinating features are the obvious importance of allergy in most cases and the complete disappearance of attacks with pregnancy, in fever or with abscess formation. The main reason for mentioning asthma is that in a proportion of cases (about 20%) disease of the nasal sinuses appears to be the major cause of attacks.

The Causes of Asthma.

It is essential to distinguish between precipitating causes and predisposing causes, because asthma may not occur unless both are operating. Take for instance the patient who has attacks only in the early summer. Skin tests reveal large reactions to grass pollens, attacks disappear at the seaside, and desensitization with a pollen extract causes attacks to cease for some years. Surely then pollen is the cause of the attack! Unfortunately one can point out hundreds of other subjects, equally sensitive to pollen, who suffer only from hay fever and no asthma on exposure to pollen. One must assume, in addition, a nervous instability or hyperresponsiveness which allows the allergic stimulus to precipitate the attack. We must assume then that all asthmatic patients are unduly responsive to stimuli, and it becomes understandable why such a variety of stimuli can precipitate attacks. These stimuli may be exposure to allergens, infections, reflex effects from sinus disease, bronchi, gall-bladder, uterus *et cetera*, or psychological stress.

Types of Asthma.

There are three types of asthma—extrinsic, intrinsic, and that due to food or drug sensitivity.

In 80% of cases air-borne allergens precipitate attacks of asthma, and this is said to be of the "extrinsic" type. Season and environment affect these patients, and skin tests give positive results.

In 20% of cases air-borne factors are of no importance, and infection, reflex effects from nasal sinuses *et cetera*, are of major importance (intrinsic type). Skin tests give negative results and symptoms are unaffected by season or environment, except that a warm, dry atmosphere helps most asthmatics.

Some asthmatics are sensitive to certain foods or drugs.

Hypersensitivity to Aspirin.

About 2% of asthmatic patients are intolerant of aspirin, and violent attacks and even death follow ingestion of small doses. The curious thing is that almost all these aspirin-sensitive patients have nasal polypi, and many of

them could take aspirin without harm before the polypi developed. Alexander Francis described these cases as early as 1903, and he stated that if an asthmatic patient had nasal polypi, a low blood pressure and intolerance of aspirin, no treatment would cure him, and any nasal operation would make him worse ("Francis's triad"). My experience fully confirms this dictum; but Frank Coke in London claims success from the use of autogenous vaccines, and some American workers with wide experience deny any special difficulty with these patients. However, in twenty years I have not seen one patient of this type benefited by nasal surgery, and I have seen several who became immediately and permanently worse, so that I am chary of recommending any operation in these cases. It is not uncommon to see aspirin-sensitive patients whose first attack of asthma followed an operation for polypi.

These gloomy remarks apply, of course, to this limited group of asthmatics. In many patients dramatic relief follows the washing of mucopus from an infected antrum or the gentle removal of a mass of polypi.

While types of asthma are being discussed, it is necessary to point out that the pattern of the disease tends to change with each decade, and that the uncomplicated, intermittent asthma in youth is different from that seen after the age of fifty years, when complications such as chronic infection and sinus disease and changes in the lungs tend to make attacks more severe and almost continuous.

Investigation.

In the investigation of asthma, a well-taken history is of the greatest importance, and one must decide as soon as possible the type of asthma with which one is dealing. Inquire especially as to the age and mode of onset and the effects of season or changes of environment, and whether relatives have allergic diseases. Other important investigations include general examination, tests for allergy, X-ray examination of the sinuses and chest, and an opinion from a rhinologist. In performing skin tests it is of great importance to have really reliable reagents, and although the technique of testing is simple, some training is necessary. Scratch tests with really potent extracts of allergens give precise information. Intradermal tests can be dangerous, are more painful and more expensive, and may be misleading, as some extracts produce non-specific irritation which by the inexperienced is interpreted as a positive reaction. Most patients react to several different allergens, but when a technician constantly reports dozens of reactions for each patient, one can be sure that his technique is faulty. Once one has found what the patient reacts to, it is necessary to try to assess the significance of each reaction by referring again to the history.

Treatment.

The main points in treatment are to avoid the appropriate allergens, to desensitize the patient if allergens cannot be completely avoided, to deal with complications such as naso-pharyngeal disease, to establish a healthy routine with regard to exercise *et cetera*, and to see that the diet is well balanced. Symptomatic remedies such as adrenaline, ephedrine and aminophylline are prescribed. Iodides have a curiously useful action in some cases, and in a few, prolonged use of iodides appears to be curative. When attacks are precipitated by recurrent infection, sulphonamides or penicillin are extraordinarily helpful in aborting attacks, especially in children. In rare cases I have seen apparent cure follow a full course of sulphadiazine; but generally this drug produces improvement for only a few weeks. Vaccines, of course, are most effective in some cases.

Some authorities, especially in America, used to regard allergy to foods as an important factor in asthma and vasomotor rhinitis, but it appears to be of minor importance in Australia. However, one occasionally finds a case in which dramatic improvement follows the omission of one or two foods, and cow's milk is one of the commonest offenders. One trouble is that skin tests with foods are generally unsatisfactory, partly because many of the extracts of foods are unstable, feeble, and sometimes irritant. Even when extracts of known potency are used, an allergic patient may not give a positive response to a skin test. Elimination diets or a diary give more positive information, but they can be used only when symptoms are constantly present.

CHRONIC NASAL DISEASE.

If one excludes injury and anatomical defects, it appears that the chief factors leading to chronic nasal disease are infection and the effects of allergens in hypersensitive subjects. Other possible factors are faulty diet, exposure to fumes and dusts, emotion, stasis, and metabolic and endocrine upsets. Monkeys and some other animals show changes in the nasal mucosa during the sexual cycle, and it is quite possible that endocrine disorders and perhaps prolonged psychological stress can cause changes in the human nose. It is conceivable, too, that certain tissue defects are inborn, and although in youth the nose may be healthy, abnormal changes are destined to appear at some later period. No doubt pathologists in the future will be amused at our efforts to explain almost all conditions as effects of either infection or allergy.

Differential Diagnosis.

The results of infection are distinguished from those of allergy by the history, clinical examination, radiological appearances, biopsy, examination of cells in the nasal mucus, and skin tests for allergy. As was stated before, symptoms in allergic cases vary with season or environment, the mucosa in many cases is pale, swollen and moist, eosinophile cells are plentiful in the nasal mucus, and skin tests produce positive reactions to allergens.

When infection is the major factor, the mucosa is often reddish; environment has no effect, nor does season, except that these patients' condition tends to be worse in cold weather. Skin tests with allergens give negative results, and the nasal secretion contains polymorphonuclear cells. In a proportion of cases, a mixture of allergy and infection is present.

Infection.

When pus or mucopus can be washed out of an antrum or sinus, there is no dispute about infection; but it would appear that patients may respond differently to infection with any particular organism, so that staphylococci, for instance, may produce pus in one, "catarrhal" changes in another and mucosal thickening and degeneration in a third. These differences depend perhaps on factors such as nutrition, environment, previous infections, anatomical features, endocrine balance *et cetera*.

It is obvious also that different effects will be produced by different organisms, such as cocci, tubercle bacilli, leprosy bacilli, spirochætes and viruses.

It is generally considered that infection usually becomes chronic for anatomical reasons (lack of drainage or aeration *et cetera*); but immunity obviously must be important and nutrition may be equally so. I imagine that a particular organism may invade perhaps a million persons and be repelled successfully by almost all. But in a few the organism finds just precisely the food it needs, and it is able to multiply and adapt itself and resist all efforts to dislodge it.

It seems essential to suspect infection in any chronic nasal disease; various workers (especially in the United States of America) report finding tissues full of bacteria although no pus was present.

In some cases the changes are due to a mixture of infection and allergy, and in a number it appears that allergic disease actively predisposes the subject to infection.

The truth is that, although we are now skilled in dealing with most acute infections, chronic infection still defeats us. When effective remedies for all chronic infections are available, they will probably throw much light on the nature of chronic nasal disease, just as the injection of organic arsenic ("Novarsenobillon" *et cetera*) may give dramatic evidence regarding the cause of a chronic ulcer.

Allergy.

A few points about allergy should be mentioned. Hypersensitivity can be transferred from an allergic subject to the skin of a normal subject by the injection of a drop of serum or plasma from the sensitive subject. If the donor is sensitive to several allergens, this is transferred in the same degree. If, twenty-four hours later, one injects an extract of the appropriate allergen into this passively sensitized area, a weal appears. If sufficient is injected, the site becomes desensitized for that allergen, but is still sensitive to the other allergens to which the donor was sensitive. This method of passive transfer (or Prausnitz-Kustner phenomenon) has afforded a most useful weapon for research into allergic phenomena.

The allergic pattern tends to alter with age, so that in infants food sensitivity is important (eggs, milk and cereals). In young children reactions to perennial air-borne dusts (feathers, animal danders and "house dust") predominate. At about puberty sensitivity to pollens becomes commoner, and after middle age allergic phenomena tend to fade and lose their definiteness, and infection and obscure tissue changes become more important than allergy. But there are many exceptions to this general tendency, so that chronic infection and tissue changes may be important in some young children (especially after pertussis and measles), and some very old people retain exquisite sensitivity to pollens, animal danders, *et cetera*.

The eczema-asthma sequence is remarkable. An infant may develop eczema at perhaps four to six months; it becomes severe and generalized, but decreases at about eighteen months, leaving traces only on the flexures. Just as the eczema disappears, asthma appears in more than half of these infants. The remarkable thing is that a majority of these sufferers are intensely allergic to egg white in the eczema phase, and equally sensitive to horse dander or some similar air-borne allergen during the asthmatic phase. This sequence is found in hundreds of cases and must have some profound significance.

Histamine or something very similar is concerned in all allergic and anaphylactic phenomena. This chemical applied to a scratch in a normal, non-allergic subject will produce a weal indistinguishable from that produced by an allergen similarly applied in a hypersensitive subject. Injected intravenously into a guinea-pig, it imitates the "asthma" of anaphylactic shock. The lungs and epidermis contain large quantities of histamine, and an enzyme, histaminase, which powerfully destroys histamine, is found especially in the kidneys and intestinal wall of some species. These facts have led to the use of histamine in treatment, but general opinion is that results are disappointing. Histamine stimulates the secretion of hydrochloric acid in the stomach and is said to be one of the best means of producing peptic ulcer in experimental animals, so that adequate doses of alkali should be given after each dose. In 1930, I rendered guinea-pigs tolerant of histamine and anaphylaxis by injecting one milligramme every second day for ten doses; but all the animals became miserably thin and ill during the treatment.

A few years ago it was stated dogmatically that the tendency to suffer from allergy was inherited as a dominant characteristic; but more recently this has been disputed, and most authorities are cautious about the matter. My personal impression is that heredity is almost certainly an important factor. When allergic disease appears in two or three siblings, the "pattern of allergy" varies greatly in each. For instance, one child may react to egg white, another to feathers and a third to linseed, and some hold that most hypersensitivity is acquired by contact with allergens. However, when identical twins are allergic, it is found, at least in some cases, that the "allergic-pattern" is identical in both. This appears to be strong evidence in favour of the theory of inheritance of specific hypersensitivity as well as an inheritance of the general tendency to show allergic phenomena.

Desensitization by the injection of increasing doses of extracts of allergens is generally helpful, but until recently the reasons for the improvement were obscure. Now it has been shown that a "blocking antibody" is developed which interferes with the union in the tissues of antigen and antibody. This antibody can be produced just as effectively in normal subjects as in allergic persons.

Natural cures have already been mentioned; asthma and other allergic symptoms tend to disappear completely during pregnancy, during febrile illnesses or when an abscess forms, and fever therapy or the production of "artificial abscesses" has been used with success. The relief is so dramatic and sometimes so lasting that further research should pay large dividends.

It was generally assumed that all allergens were proteins, but it is now found that many allergens still produce reactions after all ordinary protein has been removed. Purified house dust allergen gives no protein reaction, and extracts remain active after being heated to 100° C. for ninety minutes; egg white still produces positive skin reactions on a majority of egg-sensitive subjects even when it has been boiled with acetic acid (20%) for ten minutes or shaken with salicylsulphonic acid (30%) for twenty-four hours. Knowledge of the chemical nature of allergens will lead to more effective methods of preparing therapeutic extracts.

NASAL POLYPI.

Nasal polypi are of interest to the physician mainly because a particularly stubborn type of asthma is associated with their presence. Apparently they cause powerful stimuli which pass up the fifth nerve to the brain and then down the vagus to the bronchiolar muscles, and in many cases no known treatment is permanently helpful. They are of interest in a meeting of this sort because the vexed question of the cause of polypi should be discussed.

In an excellent paper on the histology of nasal polypi, A. D. Gillies (1940) made the following statement:

> References to nasal polypi in standard text books are brief and often vague. They are lesions which have not attracted the attention of pathologists and even now their precise nature is in doubt and the factors leading to their appearance and recurrence are unknown.

Gillies states that these polypi are not myxomata nor are they neoplastic, and he considers that they are all inflammatory, the term being used in a broad sense to include phenomena associated with hypersensitivity.

J. P. Findlay (1947) classifies nasal polypi according to cause into four types: (i) infective, (ii) allergic, (iii) infective and allergic combined, and (iv) mechanical (usually associated with deformities of the septum *et cetera*).

A discussion of details of histology and pathology would be out of place here, except that one must agree with Gillies that text-books are indeed vague, and affirm that bacteriologists have not found any bacteria to be constantly associated, and that many polypi have a large proportion of eosinophile leucocytes in the tissue spaces. In my experience only about 20% of the patients with polyposis in Melbourne yield positive results to skin tests with air-borne allergens, and in some of these, the hypersensitivity is probably not significant. Sometimes the surgeon is so certain that the patient is allergic that he feels that the skin tests were faulty; but the history almost invariably supports the idea that air-borne allergens are not a factor. If they were, the patient would fairly rapidly recover on moving to an environment where the air was really clear, or his condition would improve at certain seasons.

Of course there is still a possibility of allergy to foods, drugs, hormones or even unusual metabolic products, and, occasionally, elimination of some food, such as milk, wheat or egg, produces improvement. In practice, time and expense are important factors, and it is usually impossible to test the patient with every possible substance. My feeling is that infection is still the most probable cause of polypi, and the question should be again reviewed by a competent bacteriologist, as methods have improved greatly even in the past decade. In the tropics certain organisms such as rhinosporidia definitely cause polypi, and we should look again for specific bacterial

and virus factors. I understand that nasal polypi occur fairly commonly in domestic animals, and attempts should be made to transfer these to healthy animals of the same species.

One interesting suggestion is that the œdema which precedes polypus formation is the result of chronic lymphatic obstruction, and it is held that constant pressure from a balloon introduced into the antrum will cause small polypi to disappear, although they tend then to appear in adjacent regions.

Recently J. P. Findlay (1947) described a series of 40 patients treated with radium. He claimed 36 successes, and stated that in no case did necrosis of bone or cartilage occur.

When a patient reacts definitely to some allergen, avoidance of the allergen and desensitization sometimes appear to produce retrogression of the polypi. When no allergic clue is found, the physician has no clear indications for treatment. Occasionally an autogenous vaccine is helpful, and in others staphylococcus toxoid has seemed useful. But, when the causes are unknown and the prognosis is uncertain, one feels hesitant about embarking on a prolonged course of treatment. If further studies show that a proportion of polypi are infective, chemotherapy may some day provide a swift remedy.

I would conclude this section on polypi by repeating that existing knowledge on the subject is scanty, that research is badly needed, and that a majority of patients fail to show signs of allergy to air-borne allergens. Nor does the history suggest this type of allergy as a cause. And I would reemphasize the risks of precipitating intractable asthma by radical operation in these cases, especially if there is intolerance for aspirin.

Special Problems.

Three special problems need to be discussed: (*a*) How can the physician assist in the treatment of the chronically "nosey" individuals complaining chiefly of obstruction or "colds", in whom the rhinologist can find no clear evidence of infection or indications for treatment? (*b*) How can the rhinologist help with the treatment in those numerous cases in which the physician believes that chronic nasal disease is the cause of severe and persistent non-allergic asthma? (*c*) Why does a skilfully performed operation on the nose sometimes fail to give relief?

If an allergic clue is found, the removal of the allergen or, if necessary, desensitization, is generally effective. But results are poor, even in allergic cases, if gross exposure to the allergen continues, if the patient is sensitive to a large variety of allergens, or if for some reason he is unable to develop antibodies in response to treatment. If no allergic clues are found, the cause of the disorder usually remains obscure, the surgeon feeling that some allergic clue has been missed, and the physician feeling that some sort of atypical infection is the cause. A majority of these patients are rather worse in cold weather, but otherwise changes of environment and season do not alter the symptoms. As with polypoid disease, symptoms at times disappear spontaneously, sometimes after prolonged treatment with a carefully made autogenous vaccine, and in a few cases staphylococcus toxoid appears to have been helpful. Neurosis is not uncommon, and if a careful examination reveals no gross disease, an optimistic report and firm reassurance often work wonders. No doubt the disorder in some cases is due to the more obscure factors discussed earlier in this paper.

On the other hand, the physician must appeal to the rhinologist for help for those numerous patients (usually aged over forty years) in whom chronic chest disease appears to be due to chronic sinus disease. Prolonged observation convinces him that the condition of these patients will never improve until the sinus disease is remedied; and yet bitter experience of some unfortunate patients warns him that surgical interference can sometimes make things disastrously worse. His constant insistence on these failures is apt to scare the surgeon off any interference at all; but in my opinion, if infection is the only factor, an attempt should be made to clear it up in selected cases. It is a curious fact that any operation tends to relieve symptoms for a few months, and a good follow-up system seems essential if we are to assess results and thus obtain guidance for future decisions. Sulphonamides and penicillin produce transient but definite improvement in many cases of infection, and I have seen at least one lucky patient in whom full doses of sulphadiazine given two years ago for an infected hand caused complete disappearance of asthma and sinusitis. Apparently in this case a susceptible germ was easily accessible to the drug and was completely killed.

Surgical operations on sinuses often fail because the possibility of an allergic factor has been forgotten.

One of my medical friends was operated on some years ago in December for "pansinusitis", and ten months later he had asthma for the first time together with severe nasal symptoms. It was then found that he had had "sinusitis" each year in November and December, skin tests revealed pronounced sensitivity to grass pollens, and desensitization gave much relief.

In all cases inquiry should be made about the effects of season and environment, and if there is any doubt, the patient should take a holiday for a few weeks. If symptoms disappear the inference is obvious. The ideal would be to test every patient before any major nasal operation with a selection of the ten most important allergens. Surgical treatment of allergic patients often makes matters much worse, and desensitization often produces poor results if there are residual infection and scarring from operations.

Research.

Obviously we badly need well organized research on these important problems. The ideal would be a team consisting of a pathologist, a physician, a rhinologist, a bacteriologist, a physiologist and a secretary who could follow up each patient. The obvious difficulties would be to provide money, suitable accommodation and trained personnel with adequate time for these studies. However, these problems are important and a solution is unlikely unless an organized attack is made.

Conclusion.

Chronic respiratory disease appears to be due largely to the effects of infection and allergy, and the prevalence of these disorders is probably due mainly to novel and adverse changes of environment and methods of living.

It is often difficult to assess the relative importance of infection and allergy, and well planned research and a "follow-up" system are needed to improve methods of diagnosis and treatment, and perhaps to define other important causes of which we are ignorant at present.

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Reports of Cases.

CARCINOMA OF THE DUODENUM.

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Clinical Record.

A WOMAN, aged fifty-seven years, was referred to me in August, 1947, for a gastro-intestinal examination. She gave a history of undue fatigue and vague indigestion, with slight discomfort after meals and relieved by food; additional symptoms were flatulence and constipation. Her appetite was fair and she had lost no weight. The symptoms extended over about twelve months.

The clinical examination revealed no abnormality.

An opaque meal was given. This entered the stomach naturally, and no residue or secretion was present. The

tone of the stomach was good and the outline of that organ as far as the pylorus was sharp and regular. The food left immediately and rapidly. The duodenal cap was distorted; it did not distend or contract. The appearance was similar in all the films, which also showed some slight irregularity at the greater curvature side of the pyloric segment (Figure I).

In five and a half hours' time a small residue was present in the stomach, the rest of the opaque food being in the small coils in the pelvis and in the colon, from the caecum to the splenic flexure. The caecum was normally movable and no abnormality was visible in the colon.

From this examination, which revealed absence of distension of the duodenum together with gross irregularity and half shadows, I concluded that the patient had a carcinoma of the duodenum. Infiltration at the extreme prepyloric area was also present; this evidently caused the pylorus to gape, and accounted for the rapid initial passage of the food from the stomach. The duodenal lesion was the more extensive and was evidently the primary focus, the carcinoma extending proximally through the pylorus.

Great difficulty was encountered in persuading the patient to undergo operation, and this did not take place till two months after the opaque meal examination.

The operation was performed by Dr. Kenneth Hadley; he found around the pyloric area a carcinoma, two-thirds of which extended into the stomach and one-third into the duodenum. There was evidently some perigastric and periduodenal infiltration, as the pyloric area had to be dissected from the pancreas, when partial gastrectomy and gastro-jejunostomy were later performed.

Microscopic examination of the specimen showed an infiltrating type of carcinoma extending deeply through the walls. Its tumour cells were closely packed in cords and strands and contained well-stained nuclei.

Comment.

I feel fairly certain that this was a primary carcinoma of the duodenum, and because of the delay in operating it had time to extend into the stomach.

Primary carcinoma of the duodenum is rare; and I have seen it only once before in records of over 40,000 opaque meal examinations. More frequently carcinoma in this area is found as an extension from a carcinoma of the head of the pancreas which later invades the ampulla.

HISTOPLASMOSIS: REPORT OF AN AUSTRALIAN CASE.

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HISTOPLASMOSIS is the disease caused by infection with *Histoplasma capsulatum*, a fungus which was discovered and named by Darling, who described three cases he had found in Panama in 1905 and 1906. The disease was not reported again until 1924, but since then there has been a progressive increase in case reports. Up till 1946, over eighty cases had been reported, of which the great majority were in the United States of America. Other countries where histoplasmosis was discovered were Brazil (eight cases), Panama (three cases), Argentina (two cases), and Mexico, British Honduras, England, Austria, South Africa, Java and the Philippine Islands (one case each). It has not previously been reported in Australia. Good recent reviews of the subject are those of Parsons and Zarafonetis[1] and of Ziegler.[2]

Mycology.

Histoplasma capsulatum is unique among pathogenic fungi, in that it parasitizes cells of the reticulo-endothelial system, though this peculiarity may be primarily a host defence mechanism. It is rarely found extracellularly. In the lesions it appears as small round or oval bodies, 1·0μ to 5·0μ in diameter, with an average diameter of 3·0μ. The bodies have a definite hyaline capsule, the chromatin mass is irregular in distribution, and sometimes a large vacuole is seen within the cell body. It stains well with ordinary dyes, and is weakly Gram-positive and slightly acid-fast. At first thought to be a protozoon, it differs from Leishmania in having no kinetoplast and in being less regular in size and shape. Occasionally budding forms are seen in tissues.

Histoplasma capsulatum grows well on media such as blood or serum agar and Sabouraud's glucose agar. Yeast forms grow at 37° C., but at room temperature the fungus reverts to mycelial form, showing septate and branched hyphæ bearing small spores.

Most laboratory animals are susceptible, and dogs, ferrets, rats and mice have been found to be infected naturally. Since *Histoplasma capsulatum* has never been found free in nature, it is probable that certain domestic animals are reservoirs; but the epidemiology of the disease is little understood.

Man may be infected through the skin or mucous membranes, or by ingestion or inhalation of the fungus.

Clinical Features.

The manifestations of histoplasmosis vary, particularly in relation to age, portal of entry and extent and rate of dissemination.

Of recorded cases 20% are in infants. In them infection usually occurs by the intestinal route, generalization is rapid and the duration of life rarely exceeds several weeks.

Adults usually die after three to eight months.

If infection occurs through the skin, nose or mouth, the initial lesions are papules, granulomata or ulcers. Growth is generally slow and localized at first, but sooner or later, if the condition is untreated, secondary lesions are likely to occur; the regional lymph glands are invaded and wide dissemination follows.

As reticulo-endothelial cells exist in every part of the body, the systemic form of histoplasmosis has protean manifestations and can mimic many diseases. The pathology is that of an infectious granuloma.

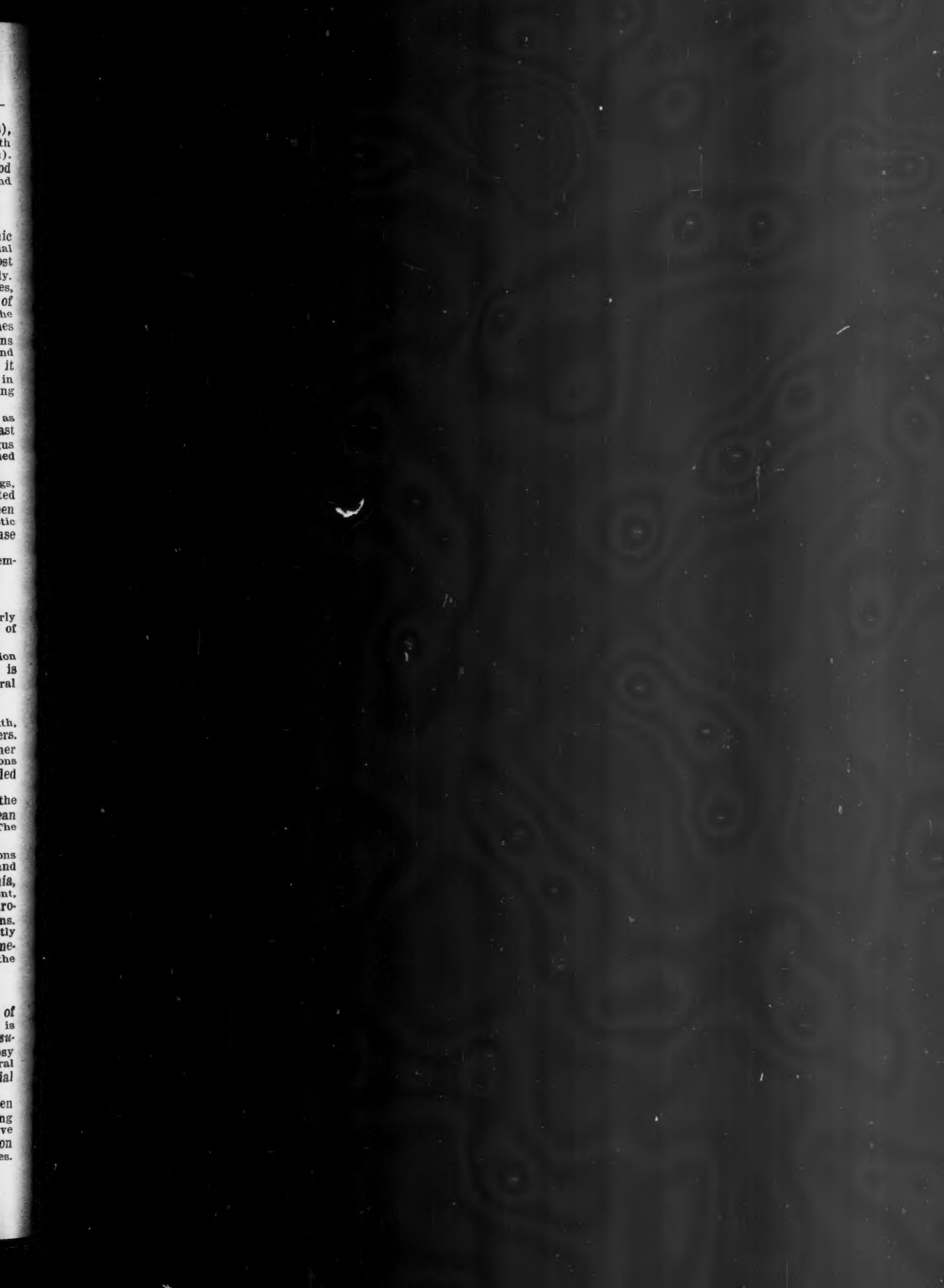
In an analysis of 61 cases of histoplasmosis, Parsons and Zarafonetis found that the most prominent signs and symptoms, in order of frequency, were fever, anæmia, hepatomegaly, splenomegaly, lymph gland enlargement, leucopenia, lesions of the lung, lesions of the gastro-intestinal tract, ulceration of the pharynx and skin lesions. At autopsy the lungs and suprarenals were frequently found to be involved. One patient had endocarditis. Sometimes healing occurred in the primary lesions while the disease extended elsewhere.

Diagnosis.

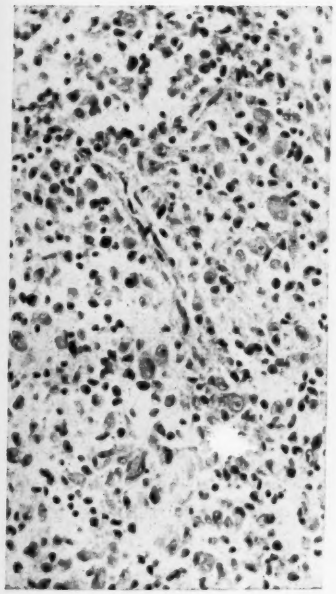
The diagnosis may be indicated by the appearance of the lesions and by the patient's signs and symptoms, but is established only by demonstration of *Histoplasma capsulatum* in the tissues or discharges by swabbing, by biopsy or by puncture of sternal marrow or lymph nodes. Cultural examination or animal inoculation of suspected material should always be performed when possible.

In the United States, a histoplasmin skin test has been developed, diluted sterile filtrates of broth cultures being used. Failure to react is of some value; but a positive result can be misleading, as it may be due to sensitization to allied fungi or to yet undetermined antigenic substances.

[1] The present authors were not directly associated with this case. The patient was examined by Dr. H. R. G. Poate, and the microscopic sections were first examined by Dr. A. E. Finckh, before being forwarded to Dr. (now Professor) A. J. Canny and Dr. T. Vickers, of the Kanematsu Institute, Sydney Hospital. Our interest results from the receipt of a slide of the lesion generously presented by Professor Canny. We have prepared this report with the consent of the principals and are grateful also to Professor H. J. Willinson for the photomicrographs.



ILLUSTRATIONS TO THE ARTICLE BY Dr. R. D. K. REYE.



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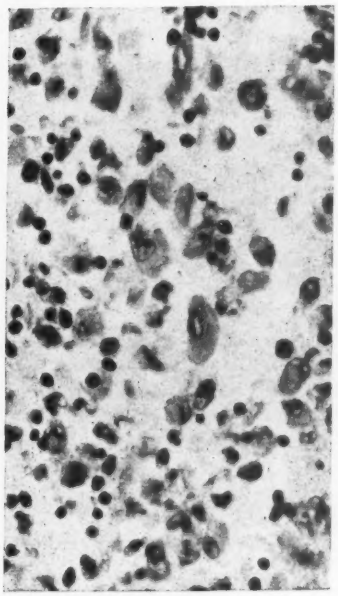

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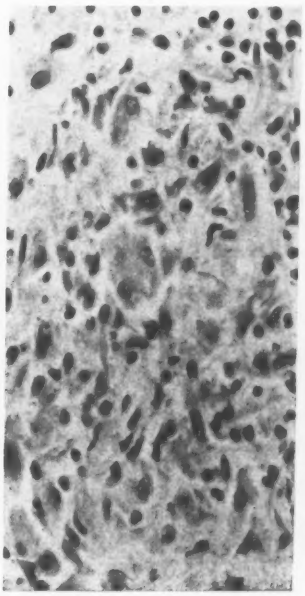

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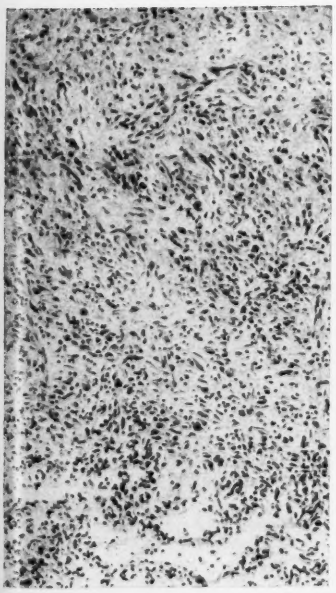

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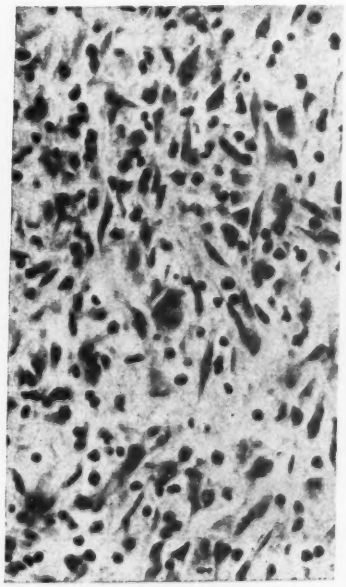

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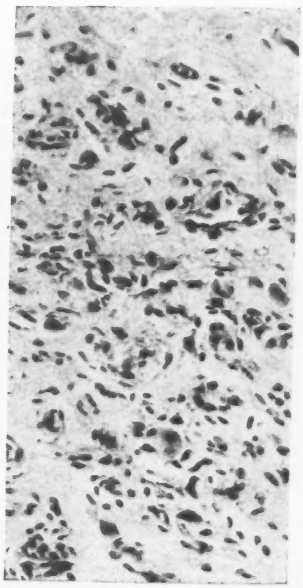
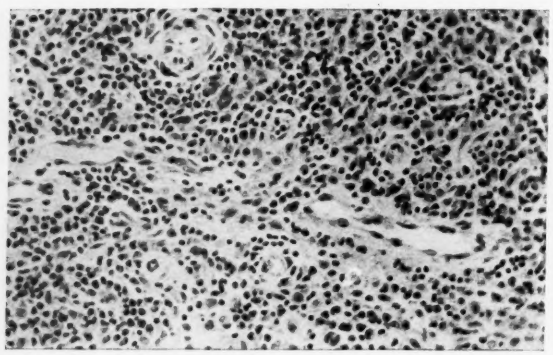


Figure VI.

ILLUSTRATIONS TO THE ARTICLE BY Dr. R. D. K. REYE.



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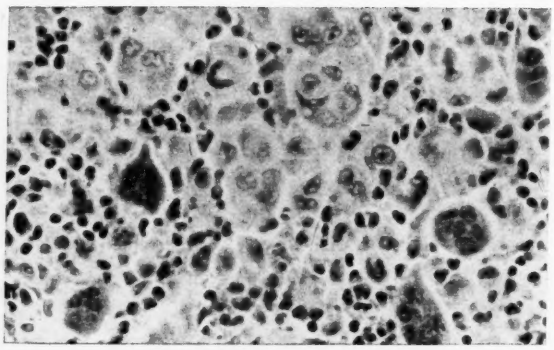

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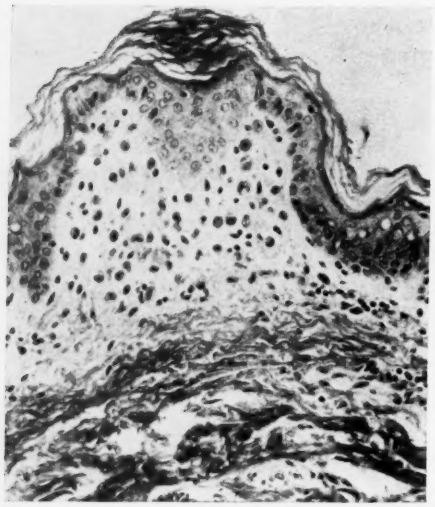


Figure IX.

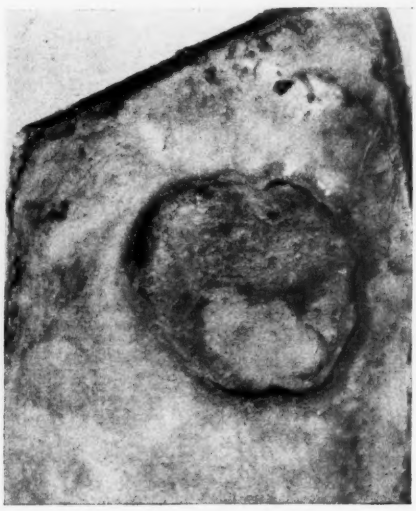
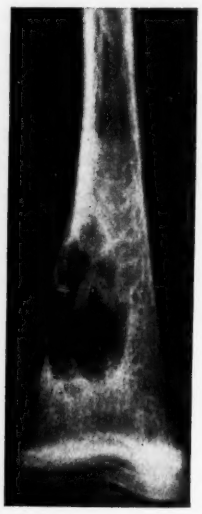


Figure X.



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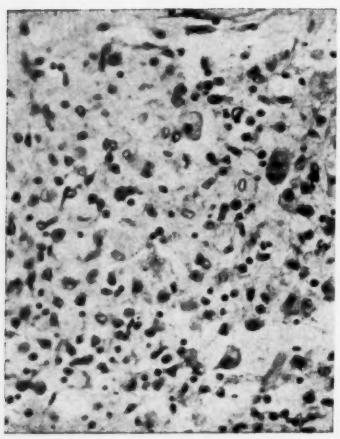

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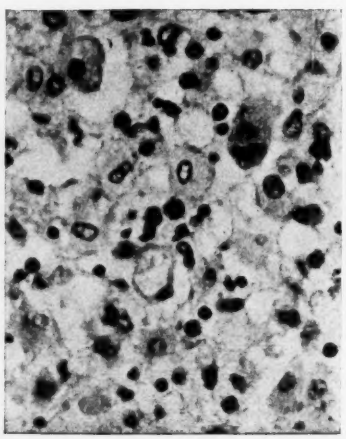

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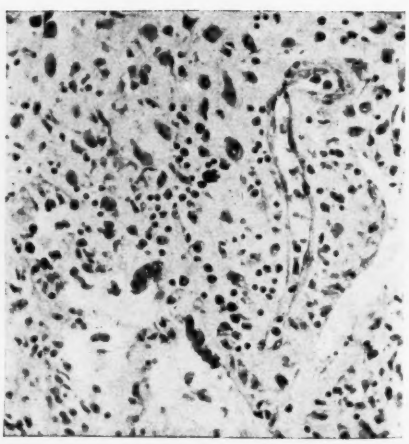


Figure XIV.

ILLUSTRATIONS TO THE ARTICLE BY DR. H. M. HEWLETT.

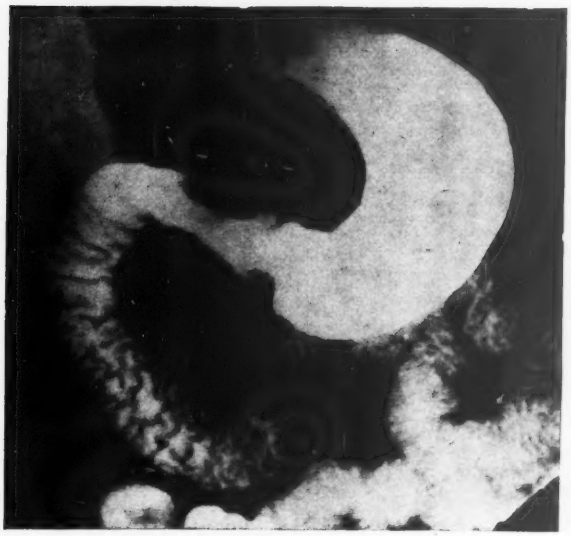


FIGURE I.

ILLUSTRATIONS TO THE ARTICLE BY DR. D. W. JOHNSON AND DR. E. H. DERRICK.

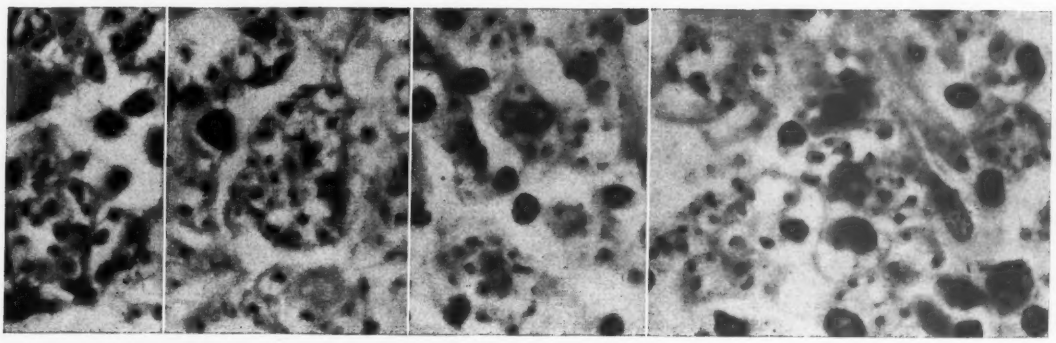


FIGURE II.

Composite photomicrograph from the centre of the lesion, showing numerous histoplasma parasites within large mononuclear cells. Some of these with capsules can be seen in the left lower corner (× 825).

ILLUSTRATIONS TO THE ARTICLE BY DR. JEFFERY R. TRIPP AND DR. R. D. ROTHFIELD.

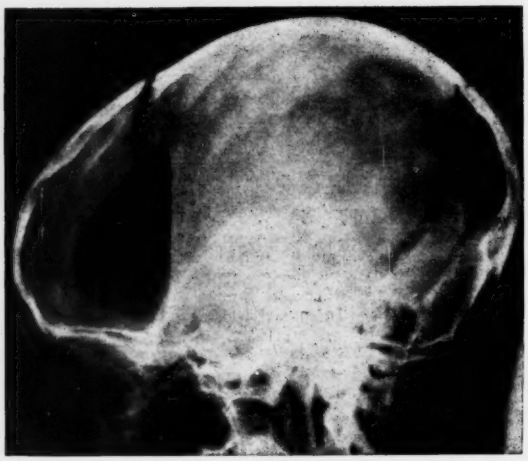
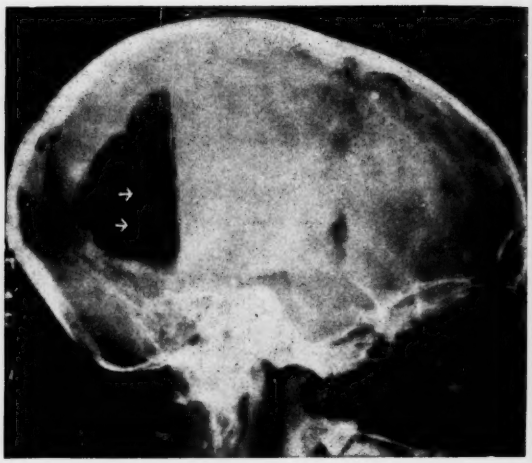


FIGURE I.



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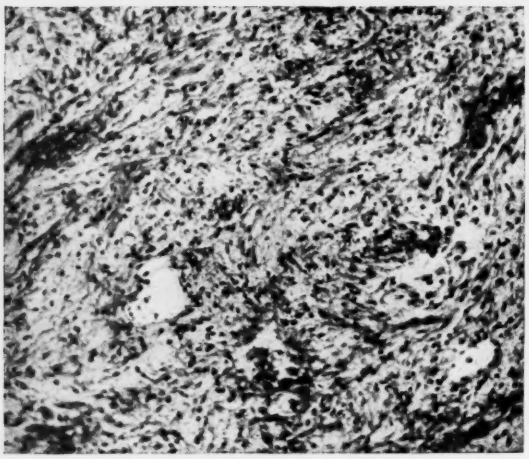

FIGURE VI.

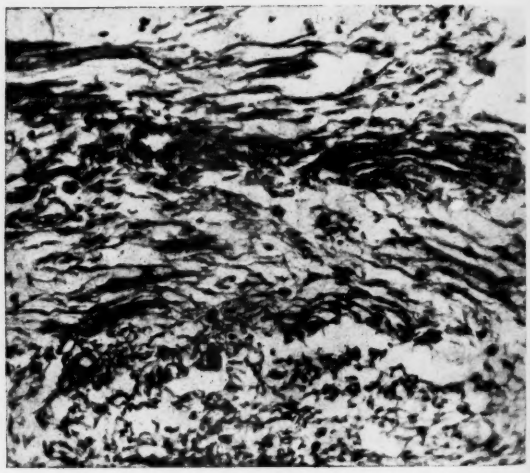

FIGURE VII.

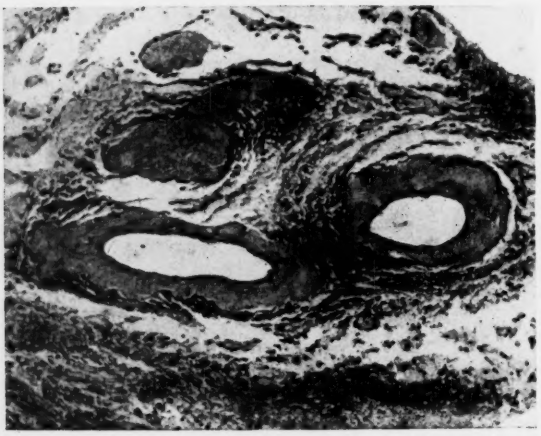

FIGURE VIII.

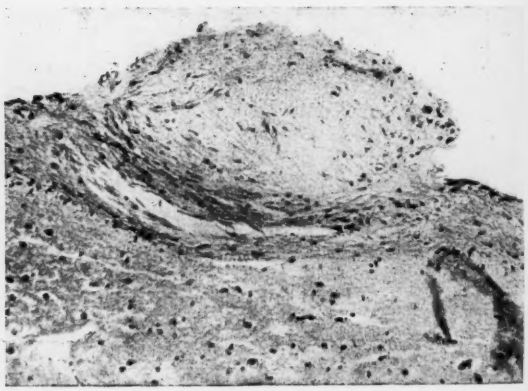

FIGURE IX.

The lesions of histoplasmosis must be distinguished from carcinoma, gumma, primary syphilis, sarcoidosis, *tuberculosis cutis*, leuchæmia, leishmaniasis, moniliasis, rhinosporidiosis, chromoblastomycosis and sporotrichosis.

Prognosis.

Histoplasmosis is almost always fatal. Of the 61 cases analysed by Parsons and Zarafonetis, only four patients were alive after two to six years, and three of these had tongue ulcers. More recently, Curtis and Grekin[3] reported two patients alive approximately two years after sulphadiazine therapy.

Yet the prognosis of histoplasmosis may not be so black as the recorded cases would indicate. It may repeat the history of many diseases that were at first known only from fatal cases. Several authors have postulated a subclinical grade of infection to explain the large number of reactors to the histoplasmin test who appear in good health. Further, some autopsies have disclosed evidence of healing by fibrosis.[5]

Treatment.

If there is no evidence of spread to regional lymph glands or other organs, radium therapy or excision of the primary lesion may be curative. Parsons and Zarafonetis cite a case of apparent therapeutic success with "Neostam" (stibamine glucoside); but "Neostam" and "Neostibosan" have not effected a cure in other cases.[4] Curtis and Grekin[3] have had apparent success in two cases with large doses of sulphadiazine (six grammes daily for ninety-six and eighty-seven days respectively).

Clinical Record.

Mr. B., aged fifty-one years, was a farmer. He owned a mixed farm in the Orange district of New South Wales, and had never been outside Australia. On October 21, 1943, the patient consulted Dr. H. R. G. Poate about a lump which had developed on the left side of his chin over a period of three months. Clinically, the lesion resembled a basal-cell carcinoma. It was raised one or two millimetres above the surface of the skin, and had a diameter of five millimetres, was quite round in outline, and had never discharged or ulcerated. The tumour was excised widely under local anæsthesia and healing was normal.

Dr. Poate informs us that in December, 1947, the patient was well and had had no recurrence. No member of his family and no friend is known to be affected.

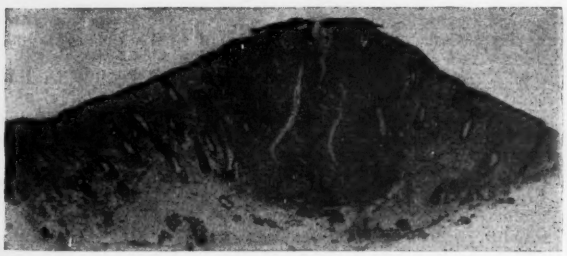

FIGURE I.

Cross-section of the whole lesion, showing a granulomatous nodule in dermis (× 4·5).

Histological Examination.

The material for examination consists of a slide stained with hæmatoxylin and eosin.

The lesion extends from the cutaneous surface through the dermis to the subcutaneous tissue (Figure I). In section it appears approximately circular in shape and about six millimetres in diameter. The surface bulges over it, but the epithelium is intact except for a minute area of ulceration at the summit.

The central part of the lesion consists of a large number of large mononuclear cells containing parasites (Figure II). They lie in the cytoplasm and often are surrounded by a clear space which may be due to shrinkage. Some cells contain only a few; others are grossly distended by the multiplied parasites. Capillaries are numerous and inflammatory cells are scattered throughout. Towards the circumference the parasites become less numerous.

The lesion is surrounded by a defensive zone of granulation tissue. Its cells are mainly large mononuclear cells; fibroblasts, neutrophile leucocytes, lymphocytes, foreign body giant cells and plasma cells also occur. In the subcutaneous aspect of the circumference there is considerable formation of collagen; laterally the fibroblastic reaction is much less and the barrier to the spread of infection less satisfactory.

The parasites are usually rounded or oval in shape; the majority measure about 3·0μ to 4·0μ in diameter, though some extra large forms reach 8·0μ. The substance of the parasite stains with hæmatoxylin, usually in a finely speckled manner. In most parasites there is a more densely stained spot resembling a nucleus. Sometimes the stained material is crescentic or irregular in shape; this may be due to distortion in the preparation of the section or to degeneration. Many parasites show a clear, colourless or pink-staining capsule. It is more evident in the larger individuals, in which it is about 0·5μ thick. No budding forms are to be seen, but some parasites have a pointed shape which may perhaps represent incipient budding.

The general morphology of the parasite, particularly the presence of a capsule, and the location within the large mononuclear cells, identify it as *Histoplasma capsulatum*.

Comment.

A noteworthy feature of this case is that the patient has remained apparently free from the disease for four years since the lesion on the chin was excised. This is cause for congratulation and hope; but one should hesitate before concluding that he is cured. Parasites were very numerous in the lesion and some may have spread beyond it.

It was not possible to investigate this case by cultural methods, but we believe that the appearance of the fungus in the section is sufficiently characteristic of *Histoplasma capsulatum* to leave no doubt as to the diagnosis.

References.

(1) R. J. Parsons and C. J. D. Zarafonetis: "Histoplasmosis in Man: Report of Seven Cases and a Review of Seventy-one Cases", *Archives of Internal Medicine*, Volume LXXV, 1945, page 1.

(2) E. E. Ziegler: "Histoplasmosis of Darling: Review and Case Report with Autopsy", *Annals of Internal Medicine*, Volume XXIV, 1946, page 1073.

(3) A. C. Curtis and J. N. Grekin: "Histoplasmosis: A Review of the Cutaneous and Adjacent Mucous Membrane Manifestations with a Report of Three Cases", *The Journal of the American Medical Association*, Volume CXXXIV, 1947, page 1217.

(4) "Queries and Minor Notes", *The Journal of the American Medical Association*, Volume CXXXV, 1947, page 543.

(5) N. F. Conant *et alii*: "Manual of Clinical Mycology", 1944, page 151.

A CASE OF BASILAR IMPRESSION ASSOCIATED WITH CEREBRAL TUMOUR.

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AND

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BASILAR IMPRESSION is a deformity of the occipital bone associated with narrowing of the *foramen magnum* and of the cervical canal, which gives rise to progressive compression of the spinal cord, medulla and cerebellar hemispheres.

Causes.

The condition may be secondary to skeletal disease in which decalcification and softening of bone occurs—that is, Paget's disease, hyperparathyreoidism, osteomalacia *et cetera*. It may also be secondary to a chronic increase of intracranial pressure, causing thinning of the calvarium and the basi-occiput. This type is not usually associated with abnormalities of the cervical vertebræ. The condition may also be due to congenital atlanto-occipital malformation. In these cases there are usually fusion, or "assimilation", of the atlas to the occiput, deformity of the *foramen magnum*, and flattening of the base of the skull (platybasia).[1] The arch of the atlas may be defective or absent and other cervical vertebræ fused or missing (the Klippel-Feil deformity).[2]

Features of the Condition.

The patient presents a typical "bull neck" with forward carriage of the head, but movements of the head on the neck are usually not limited.

There may or may not be associated symptoms, and these, when they occur, are due to compression of the contents of the posterior cranial fossa or to stretching of the cranial nerves or spinal cord.

Any combination of the above features may occur, simulating many neurological syndromes. Cerebellar degeneration, syringomyelia, syringobulbia, bulbar palsies, syndrome of Klippel and Feil or disseminated sclerosis may be erroneously diagnosed; later, when obstruction of cerebro-spinal pathways gives rise to hydrocephalus, the condition may be mistaken for cerebral or cerebellar tumour.

Diagnosis.

Although there are many characteristic clinical manifestations in this condition, the final diagnosis depends on the demonstration of the characteristic X-ray appearances. These findings were first described by Schüller,[3][4] in 1911 as follows:

> In the lateral view the malformation, the rudimentary development and the dislocation of the cervical vertebræ . . . are well shown.
>
> The most striking detail is, as a rule, the abnormal appearance of the lines of projection corresponding to the basilar and condyloid portion of the occiput; instead of forming concave arches, as in normal cases, these lines are convex toward the cranial cavity ("convexo-basia") and continue backward in the form of a deep concavity to the squamous portion of the occiput. Therefore, the outlines of the floor of the posterior fossa . . . are characterized by their S-like curvature in cases of "basilar impression".

Chamberlain[5] aroused interest in the clinical condition and described a further radiological diagnostic point in that, in the lateral skiagram of the skull, the odontoid process and the body of one or more cervical vertebræ lie above the line drawn from the posterior edge of the hard palate to the dorsal lip of the *foramen magnum*—the so-called "Chamberlain line".

Occurrence.

Ebenius[6] described four cases associated with neurological changes.

Chamberlain[5] described four cases, in two of which symptoms were present.

Ray[7] points out, from an analysis of twelve cases, that operation for the relief of symptoms should be directed at decompression of the upper cervical cord and posterior fossa by wide removal of the occipital bone and laminectomy of the first and second cervical vertebræ; he further states that the dura must be opened to obtain satisfactory decompression, and that the less intradural manipulation of nervous structures the better.

Craig, Walsh and Camp[8] (1942) present three cases, with widely varied clinical features. Their first patient was a male, aged forty-six years, with evidence of involvement of mid-line cerebellar structures, and with paresis of the right fifth and the left seventh and twelfth cranial nerves. Their second patient was a male, aged fifty-two years, with optic atrophy, and with weakness and numbness of the legs. The third patient was a male, aged sixteen years, with long-standing respiratory disturbances, difficulty in deglutition, and clumsiness of the hands. Operation on these patients produced relief in each case.

Gustafson and Oldberg[9] described five cases, two of which were associated with abnormality of the atlas. In four cases the spinal cord showed changes resembling syringomyelia, and in the fifth—that of a child, aged four years—internal hydrocephalus was present.

Moreton[10] reviews 139 cases in the records of the Mayo Clinic, in 98 of which neurological symptoms were present. Six of these patients suffered from Paget's disease of the cranial bones without involvement of the cervical vertebræ. The author states that the surgical treatment is directed to the relief of increased intracranial tension and to the relief of pressure on the cerebellum and the "vital centres". Throughout the literature we could find no record of basilar impression associated with intracranial neoplasm, and it is for this reason that this case is considered of sufficient interest to warrant publication.

Clinical Record.

The patient, a girl, aged seventeen years, was referred by Dr. R. G. Woods and Dr. T. M. Greenaway. This patient two years prior to her admission to hospital had noticed the onset of headaches. The headaches involved the whole of the head and were severe in the morning, gradually being relieved during the afternoon. Attacks of giddiness, lasting about two minutes, began two weeks later, and since the onset of the giddiness she had had headaches every day, and occasionally (sometimes every second day) she had vomited. The vomiting occurred before breakfast and was effortless, and she could then eat a normal breakfast. She had lost approximately two stone in weight. About nine months before seeking advice she had noticed that she was staggering as she walked, falling to the left. About six weeks before her admission to hospital, the patient observed that the right side of her face had become weak and that her mouth was drooping. Two weeks prior to her admission to hospital the headaches became particularly severe, and she complained that her eyesight had deteriorated and that she was "seeing double". Investigation of her past health and family history revealed nothing relevant; she was keen on sport and a good scholar. Since the onset of her symptoms, however, she had felt too ill to engage in any activity.

On examination, the patient presented extreme emaciation, a lower motor neuron lesion of the right facial nerve, bilateral papillœdema of low grade, and right external rectus paresis. The motor power of arms and legs was unimpaired; the gait was ataxic, the patient falling to the left. Romberg's sign was present, with falling to the left. Coordination was impaired on the left side and slightly impaired on the right side. The knee jerks on the left side were much exaggerated. No further neurological abnormality could be detected.

Lumbar puncture revealed straw-coloured cerebro-spinal fluid with a pressure above 300 millimetres. The cerebro-spinal fluid contained globulin in increased amount, and the total protein content was 500 milligrammes *per centum*. After the lumbar puncture the patient's condition deteriorated, and immediate operation was carried out for the relief of impending medullary compression. Under light "Avertin" anæsthesia, two occipital burr holes were made. The dura was tense and was not pulsating. The ventricles were reached at a depth of five centimetres. The cerebro-spinal fluid in the ventricles was xanthochromic and under high pressure. Twenty millilitres of air were introduced, the wounds were closed, and the patient was transferred to the X-ray department.

The films (Figures I and II) demonstrate a symmetrical internal hydrocephalus. There is pronounced "thumbing". The coronal sutures are separated. A considerable degree of basilar impression is present. The anterior, middle and posterior fossæ are in approximately the one plane. The *foramen magnum* is at least 2·5 centimetres higher than its normal position. The sella and the posterior

clinoid processes are eroded, and the angle of the clivus is 160° (Figure III). The posterior extremities of the ventricles are greatly dilated, as are the temporal horns and third ventricle. The third ventricle is rotated on its horizontal axis, and the aqueduct of Sylvius is seen running horizontally backward to the fourth ventricle.

It was concluded that basilar impression was present, and that operation for decompression of the posterior fossa was indicated.

A mid-line incision was carried down through the *ligamentum nuchæ* to the occipital bone, from which the sub-occipital muscles were freed. This procedure was rendered difficult by the presence of numerous large abnormal venous channels, and by the acute angulation of the occipital bone (see Figure II).

Dissection was continued to display the posterior arch of the *foramen magnum* and the arch of the atlas. Burr holes were made in the occipital bone and were enlarged with double-action nibbling forceps. The posterior half of the *foramen magnum* and the posterior half of the arch of the atlas were removed as far as the vertebral arteries. The thinned bone of the sub-occipital region was widely removed to form a large decompression. The dura was tense and bulging over the whole of the posterior fossa. At this stage the lateral ventricle was tapped with a Frazier needle, and on reduction of pressure the brain began to pulsate. Small openings were made in the dura over the cerebellar hemispheres, and through these openings the cerebellum was explored with a brain needle to exclude the presence of tumour of the posterior fossa. The opening in the dura on the right side was carried down past the level of the *foramen magnum* where an Arnold-Chiari malformation was clearly seen, in that the cerebellar tonsils and portion of the lower folia of the cerebellar hemispheres were found protruding through the *foramen magnum*.

The sub-occipital muscles were closed with interrupted cotton sutures and a Frazier needle was left draining the ventricles for twenty-four hours.

Twelve hours after operation the patient's condition was fair. She was conscious and responding to auditory stimuli, and no paresis of arms or legs was present. Two days after operation the patient's condition began to deteriorate; she became drowsy and was not responding except to painful stimuli. The Frazier needle was replaced. The next day the patient's condition was much the same. She was still drowsy and responded only to painful stimuli. Spinal drainage was carried out through a lumbar puncture and the pressure was reduced from 340 to 100 millimetres over an hour and a half; two ounces of xanthochromic fluid were removed and the patient's condition improved slightly. The next day her condition had again deteriorated and a further spinal drainage was performed, the pressure being reduced over two hours from 440 to 100 millimetres. The fluid had a protein content of 300 milligrammes *per centum*. Fluid had been given continuously by the intravenous route for two days, the hæmoglobin value was 9·4 grammes *per centum*, and a transfusion of 600 millilitres of whole blood was given. Four days after operation the patient's condition once more deteriorated, and at this stage, on lumbar puncture, the pressure was only 40 millimetres. The fluid was still xanthochromic and the Queckenstedt reaction was absent. An attempt was made to tap the ventricle through the previously introduced burr hole, but the ventricle could not be located. At a depth of eight centimetres firm resistance was met. The following morning, on the fifth day after operation, the patient's condition deteriorated further, her respiratory rate rose to 60 per minute, her temperature rose to 104° F., and the patient died.

Post-Mortem Examination.

The post-mortem examination (S.U. 5511) was performed twenty-two hours *post mortem* and was limited to the cranial cavity.

Skull.

On external examination, the skull was obviously of abnormal form. The portion of the occipital bone anterior to the external occipital protuberance, instead of sloping gently to the back of the neck, passed almost horizontally forwards. A large portion of the occipital bone, and the posterior arch of the atlas, had been removed at operation, but the general contour could be made out. The cranial vault was expanded and the temporo-parietal areas were more protuberant than usual. The "clivus", that slope which normally passes downwards and backwards from the *dorsum sellæ* to the *foramen magnum*, did not exist as such. From the foot of the posterior clinoid processes there ran horizontally backwards, for a distance of one centimetre, a convex shelf of densely hard bone; the

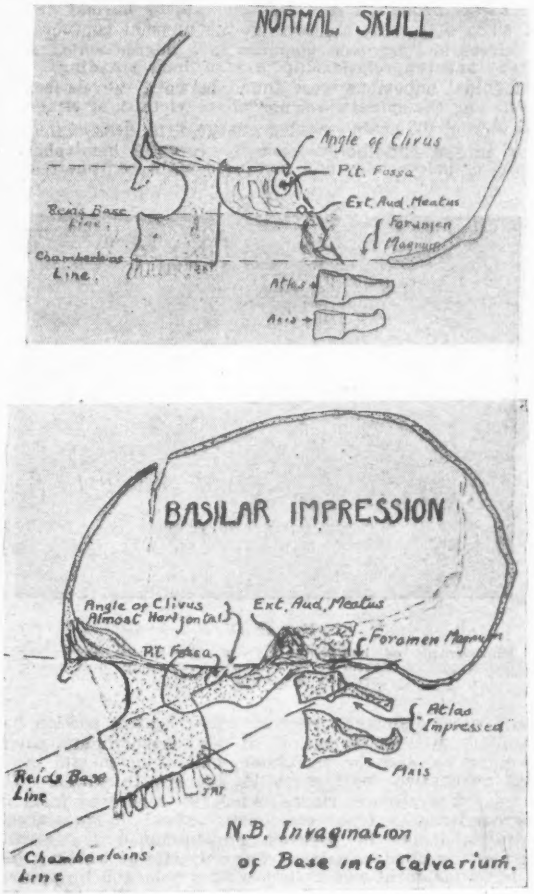

FIGURE III.

Comparative drawings, to same scale, showing normal calvarial outline contrasted with abnormalities found in this case (J.R.T.).

posterior edge of this projection constituted the anterior margin of the *foramen magnum* (Figure IV). As a result of the horizontal position of the squamous portion of the occipital bone and of the convexity of its basilar portion, the *foramen magnum* was about 2·5 centimetres above its usual level and was of reniform outline. The posterior cranial fossa was extremely shallow, and lay on approximately the same level as the middle cranial fossa. Between the two, the petrous crests rose sharply, without presenting as extensive a posterior surface as is usual. The cerebellar surface of the petrous portion of each temporal bone was directed upward rather than backward. The strikingly acute angle made with these surfaces by each aqueduct of Fallopius can be seen in Figure IV. In

addition the pituitary fossa was deeper than usual. All the bones of the cranial vault were thin, and the squamous temporal bones were of papery translucency. The greatest transverse diameter of the skull was 14·5 centimetres.

Dura Mater and Brain.

In the left occipito-parietal region there was some extradural blood-clot of operative origin associated with a burr hole. The brain itself was increased in weight (1750 grammes). The cerebellar tonsils and the lower part of the medulla passed through the deformed *foramen magnum* and lay in apposition to the spinal cord. The appearance differed from that produced by recent herniation of these structures through a *foramen magnum* of normal shape and size; they were moulded to the unusual contours of the clivus and *foramen magnum* to a degree which suggested that the relationship was of long standing. No arachnoidal adhesions were found between the cerebellar tonsils and the spinal cord, nor in the vicinity of either.

Section of the brain revealed a large, firm, fleshy tumour, lying in the mid-line between the cerebral hemispheres. It was of pale colour, and measured eight centimetres in

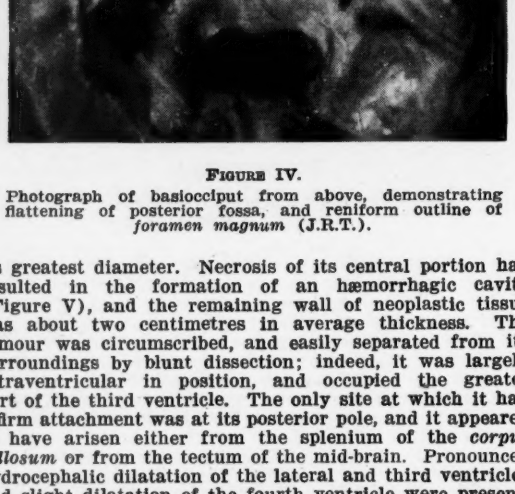

FIGURE IV.

Photograph of basiocciput from above, demonstrating flattening of posterior fossa, and reniform outline of *foramen magnum* (J.R.T.).

its greatest diameter. Necrosis of its central portion had resulted in the formation of an hæmorrhagic cavity (Figure V), and the remaining wall of neoplastic tissue was about two centimetres in average thickness. The tumour was circumscribed, and easily separated from its surroundings by blunt dissection; indeed, it was largely intraventricular in position, and occupied the greater part of the third ventricle. The only site at which it had a firm attachment was at its posterior pole, and it appeared to have arisen either from the splenium of the *corpus callosum* or from the tectum of the mid-brain. Pronounced hydrocephalic dilatation of the lateral and third ventricles and slight dilatation of the fourth ventricle were present. The ventricular system and subarachnoid space were filled with coagulated albuminous fluid. Granularity of the ependymal lining of the third and fourth ventricles was found.

Histological Examination.

The tissues were fixed in formalin, and transferred to Zenker's fluid for twenty-four hours. The stains used were hæmatoxylin and eosin, and Mallory's phosphotungstic acid hæmatoxylin.

Pathological Features.—The tumour is composed mainly of bipolar cells of piloid form. Each possesses a small ovoid nucleus, and an elongated cytoplasm, which is of uniform width throughout its length, tailing off imperceptibly to a short fibrillary process at each end (Figure VII). While definite palisade formation is not in evidence, there is a tendency towards fascicular arrangement; in some situations the cells are arranged in parallel bundles, which undulate through the section in a manner resembling fully developed isomorphic glia. A portion of the tumour exhibiting this feature is shown in Figure VI. In many areas considerable œdema is present (Figures VII and VIII). An outstanding feature of the tumour is its vascularity, but the vessels are all abnormal (Figure VIII). They are dilated, and the walls are irregular both in thickness and in structure. They stain uniformly pink with eosin, and red with phosphotungstic acid hæmatoxylin. Some of them possess a single, well-defined endothelial layer. The heteromorphic and multinucleated cells seen in a *glioblastoma multiforme* are conspicuously absent, and the vascular channels do not show the endothelial proliferation common in that tumour. The tumour is classified as a polar spongioblastoma. Its differentiation is fairly good, and its rate of growth relatively slow, approximately that of an astrocytoma rather than that of a primitive glioblastoma. Portions of the right basal ganglia and of the medulla show nothing of interest except on the ependymal surfaces, where the granulations seen with the naked eye appear as papilliform eminences, formed by the heaping up of the subependymal fibrous

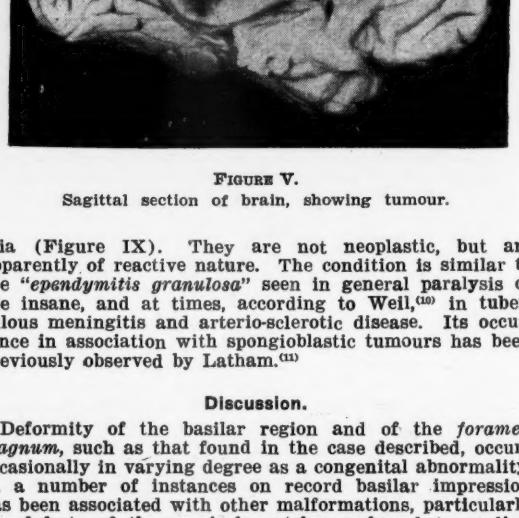

FIGURE V.

Sagittal section of brain, showing tumour.

glia (Figure IX). They are not neoplastic, but are apparently of reactive nature. The condition is similar to the "*ependymitis granulosa*" seen in general paralysis of the insane, and at times, according to Weil,[10] in tuberculous meningitis and arterio-sclerotic disease. Its occurrence in association with spongioblastic tumours has been previously observed by Latham.[11]

Discussion.

Deformity of the basilar region and of the *foramen magnum*, such as that found in the case described, occurs occasionally in varying degree as a congenital abnormality. In a number of instances on record basilar impression has been associated with other malformations, particularly the defects of the cervical vertebræ referred to earlier. Deformity of the brain stem of the Arnold-Chiari type is also usually congenital, and frequently associated with *spina bifida* or myelomeningocele. Ogryzlo[12] mentions the improbability of its production by pressure alone. There is, in fact, a tendency for all such lesions of developmental origin to appear in groups. On the other hand, cases of the Klippel-Feil syndrome occur without basilar impression, and there seems to be no reason why basilar impression of congenital origin need be invariably associated with any other developmental abnormality. In the case presented there was no fusion of any part of the atlas to the occiput, and the outline of its fully developed arch can be distinguished in the skiagram (Figure II). The protrusion of the cerebellar tonsils and the extension of the brain stem through the *foramen magnum* produced an appearance similar to that of the

Arnold-Chiari malformation; however, the leptomeningeal adhesions which form part of that lesion were absent, which suggests that the changes in the brain stem found in this case were not congenital. The deformity could have been produced by a gradual increase in intracranial pressure, portions of the cerebellum and brain stem being forced into a misshapen canal throughout the period of growth of the tumour. The result differed from the "pressure cone" seen in cases of acute cerebellar or medullary impaction.

The gross dilatation of the ventricular system distal to the tumour is sufficiently accounted for by the known tendency of tumours arising in this region to produce a "ball-valve" type of obstruction. The lesser degree of hydrocephalus found proximal to the tumour is not so readily explained. It may have been due to relatively recent obstruction of the cerebro-spinal fluid pathways at the level of the *foramen magnum* by the changes described above, and related to the sudden increase in the severity of the patient's symptoms a few weeks prior to operation. On the other hand, in basilar impression of congenital origin some degree of hydrocephalus affecting the entire ventricular system may have been present prior to the development of the tumour.

The relationship of the tumour to the deformity of the skull is uncertain. Two possibilities are to be considered: firstly, that a cerebral glioma occurred in a patient with a congenital and asymptomatic basilar impression; alternatively, that the deformity of the skull was produced by changes in intracranial pressure resulting from the presence of the tumour.

In either case the original symptoms appear to have arisen from an increase in intracranial pressure, due at first to intermittent obstruction, and later to a permanent internal hydrocephalus, into the cavity of which the tumour was able to grow without sufficiently compressing or interfering with neighbouring tracts to allow of its diagnosis or localization. The histological structure of the tumour is in keeping with its non-invasive nature, and with the prolonged course of the clinical history.

The possibility has been suggested in the literature that basilar impression may be produced by chronically increased intracranial pressure. If the changes in this case were produced by such a mechanism, then no doubt the softening of the calvarium, due to the chronic increase in pressure and thinning of the bone, gave rise to an invagination of the condyloid and basilar portions of the occiput into the calvarium, which in turn gave rise to the varied neurological signs and to the final complete obstruction of the cerebro-spinal pathways which was the immediate cause for the patient's seeking advice. The main objection to accepting such an hypothesis lies in the fact that, while slowly growing tumours in this region with gross hydrocephalus are not uncommon, no case of their association with basilar impression appears to have been recorded. For this reason it seems more likely, in the absence of clear evidence to the contrary, that the bony changes in this case were in the nature of an isolated congenital malformation.

When the pre-operative diagnosis is reviewed, it is clear that insufficient significance was placed on the greatly increased protein content of the cerebro-spinal fluid. Phillips and Goswell,[13] in their paper on cerebro-spinal fluid protein in cases of intracranial tumour, showed that a lateral shift of the cerebral axis on the brain stem is to be expected when, in the course of investigations, an increased protein content is found. In the case presented the persistent increase in protein content was considered before operation to be due to the pronounced changes in the distribution of the intracranial contents, and the disturbance of the cerebral axis to be due to the basilar impression.

However, it has been noted by Phillips[14] in two subsequent cases of milder degrees of basilar impression with associated neurological signs, that an increase in the protein content of the cerebro-spinal fluid was not found. It is, therefore, now considered that the increased protein content was due to the shift in the cerebral axis caused by the presence of the tumour.

It is unfortunate in this case that while the clinical picture was thought to be sufficiently explained by the presence of pronounced basilar impression, the tumour, which was the real cause of the train of symptoms, was overlooked, even though its posterior border is clearly seen in the ventriculograms (Figure II, indicated by arrows).

Summary.

The condition of basilar impression is discussed.

A short review of the literature is presented, and reference is made to the apparent rarity of the association of cerebral tumour and basilar impression.

A case of this unusual association is presented.

The post-mortem appearances are discussed.

The symptoms are reviewed in the light of the pathological features.

Acknowledgements.

Our thanks are due to Dr. Gilbert Phillips and Dr. T. M. Greenaway for permission to publish this case, and to Dr. Phillips for his advice and assistance. Our thanks are also extended to Professor W. K. Inglis and Dr. Oliver Latham, of the Department of Pathology, University of Sydney, for their advice and assistance in the interpretation of the pathological specimens, and to Mr. S. Woodward-Smith, of the Department of Medical Artistry, University of Sydney, for the photographs.

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Legends to Illustrations.

FIGURE I.—Lateral radiograph, brow up, demonstrating pro nounced internal hydrocephalus and basilar impression.

FIGURE II.—Lateral radiograph, brow down, demonstrating posterior edge of tumour shadow (indicated by arrows).

FIGURE VI.—Section of tumour (hæmatoxylin and eosin stain, × 100). In places the cells show a tendency towards fascicular arrangement.

FIGURE VII.—Œdematous area of tumour (hæmatoxylin and eosin stain, × 200) This area shows the elongated structure of the tumour cells.

FIGURE VIII.—Abnormal blood vessels in a vascular and œdematous portion of the tumour (hæmatoxylin and eosin stain, × 50).

FIGURE IX.—*"Ependymitis granulosa"*: the ependymal surface of the third ventricle, in the region of the thalamus, showing a typical neuroglial granulation (hæmatoxylin and eosin stain, × 100).

CRETINISM ASSOCIATED WITH METHYL THIOURACIL THERAPY.

By G. M. Hone and Ivan Magarey,
Adelaide.

Evidence of cretinism in the newborn child is uncommon except in areas of endemic goitre, but when this is associated with methyl thiouracil therapy it becomes worth reporting.

Clinical Record.

Mrs. M.S.H., aged twenty-eight years, consulted one of us on March 4, 1947, complaining of headaches present during the previous two months. She had worn spectacles for two years and had been to see an optician with the object of having her spectacles changed. She had noticed that her eyes had been a little prominent for about six weeks. The optician noticed a lump in her neck and advised her to see a doctor. She said that she had been very irritable for about two and a half months and had lost two and a half stone in weight in the last two and a half years. She had had one child three and a half years before, and her last menstrual period had appeared six weeks before the consultation.

On examination of the patient, moderate exophthalmos was seen. Her tongue was tremulous, and fullness was present about the suprasternal notch. The thyreoid gland was enlarged to about twice the normal size; it was firm, with no nodules. There was a fine tremor of her fingers and her palms were moist. She had mild tachycardia, and her blood pressure was 130 millimetres of mercury (systolic) and 88 millimetres (diastolic). She was about six weeks pregnant.

The patient was admitted to hospital. Here her hæmoglobin value was found to be 13·8 grammes *per centum*, and her white blood cells numbered 6500 per cubic millimetre. The basal metabolic rate was +53%. The galactose index was 233. She weighed 125 pounds (56·7 kilograms). The patient was thought to have mild thyreotoxicosis and to be pregnant.

On March 19 a course of methyl thiouracil was started, beginning with 0·2 gramme twice a day. There was a rapid improvement in her condition, and by April 11 she felt quite well. On April 17 the basal metabolic rate was +10% and her weight was 126 pounds (57·85 kilograms). She was discharged from hospital on April 23, still taking 0·2 gramme of methyl thiouracil twice a day.

On July 18 the methyl thiouracil dosage was reduced to 0·1 gramme twice a day, and she continued to feel well until the beginning of labour on October 26. At no time did she show any evidence of excessive dosage of methyl thiouracil. Her blood pressure remained at approximately 130 millimetres of mercury (systolic) and 88 millimetres (diastolic) all through the pregnancy. The exophthalmos diminished slightly, and the thyreoid gland became a little smaller, even though she was still taking methyl thiouracil. The resting pulse rate averaged 84 per minute.

Labour began in October 26 at 9 p.m., and a female child was born without difficulty at 1.30 p.m. on October 27 with no instrumentation. The child cried shortly after delivery, but her respirations were shallow and she was a little cyanosed from the moment of delivery. Her colour could be kept good only by the continuous use of oxygen through a nasal catheter.

At 5 a.m. the child's condition was reported as being more unsatisfactory. It was then found that the breathing was slow and irregular, averaging twelve per minute. Her pulse rate was 50 per minute. She was more cyanosed. The child also showed evidence of cretinism. The face was flat and the nose was broad with a depressed base. The tongue was large and was held semiprotruded. The fingers were short, but not unduly broad. The thyreoid gland could not be felt.

The oxygen was continued and the air passages were repeatedly sucked out. As there appeared to be an increase in intracranial pressure, the subdural space was tapped on each side through the fronto-parietal suture, but only five or six drops of blood-stained cerebro-spinal fluid were obtained at each tap. The child's condition steadily deteriorated and she died at 1.30 p.m. the same day.

Autopsy.

An autopsy was carried out by Dr. E. B. Sims.

The body was opened under water, but no pneumothorax was present. The lungs were largely atelectatic. The heart was normal. The thyreoid gland was greatly enlarged and engorged. The lateral lobes bulged round the trachea almost meeting behind. Its weight was 13·35 grammes (normal, 2·5 grammes). The aryteno-epiglottic folds were greatly thickened. The tongue was large and firm. The kidneys were lobulated with jelly-like tissue within Gerota's capsule. The suprarenals and liver were normal. When the skull was opened, much tarry blood was found over both hemispheres and in the middle and posterior fossæ. The tentorium was damaged during the removal of the brain before inspection.

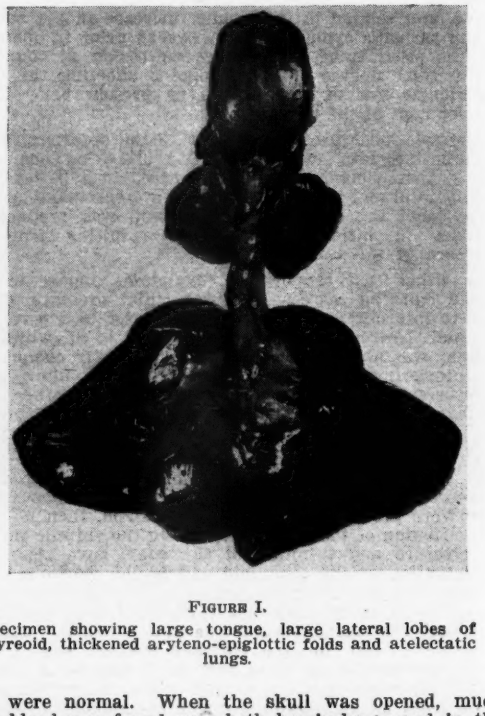

Figure I.

Specimen showing large tongue, large lateral lobes of thyreoid, thickened aryteno-epiglottic folds and atelectatic lungs.

Microscopical examination of the thyreoid revealed much vascular engorgement and increase in fibrous tissue. There was great hyperplasia of the glandular tissue, and the acini, which were lined with low columnar epithelium with central nuclei, contained no colloid. There were no areas of lymphocytic infiltration.

Comment.

It seems reasonable to ascribe the manifestations of cretinism in this baby to the effects of methyl thiouracil, because cretinism recognizable at birth is very rare indeed in this State, and also because hyperplasia of the thyreoid gland in the newborn is well known to follow the treatment of thyreotoxic mothers by this drug. Goldsmith, Gordon and Charipper[1] have also produced a condition suggesting cretinism in the offspring of a female rat which was fed with massive doses of thiourea during pregnancy.

It is known that the human fœtal thyreoid may be considerably hyperplastic by the sixth month of gestation.[2] It would therefore seem desirable that the administration of methyl thiouracil should always be

stopped before parturition and the mother helped along with iodine until after delivery. If this could be done at least three weeks before term, it should give the infant's thyreoid time to improve its condition, even though full involution of the gland might not occur for another two or three months.

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Reviews.

PHYSICAL TREATMENT IN PSYCHIATRY.

THE publication of "Sargant and Slater" in 1944 met a need for authoritative information on physical treatment in psychiatry and the success of the work was soon apparent.[1] It has been translated into Spanish and Swedish. In the 1948 edition the authors have enlisted the assistance of Dr. Denis Hill in the chapter on the treatment of the epilepsies, while Dr. W. D. Nicol has assisted with the section concerning general paralysis, and Dr. H. J. Shorvan with that concerning ether abreaction in mental exploration and treatment. The authors are emphatic that insulin coma therapy should be given within six months of the onset of a schizophrenic illness and that except in the rarest instances it is of little use in mental illness of more than two years' duration. While in selected cases the duration of illness is reduced, the tendency to relapse remains in most instances. Convulsion therapy may be used as an adjuvant to insulin-coma in schizophrenia and the authors believe that relapse rates are lower with "Cardiazol"-induced convulsions, especially in catatonic and more persistent paranoid states. The critical reader may well conclude that the choice of treatments in schizophrenic states still defies precise formulation and depends largely on the intuitive experience of the psychiatrist. In the chapter on convulsion therapy there has been included a section on the use of curare. The authors believe that curare should be given only to patients with bone disease and to those who have sustained a fracture, and not necessarily to every patient who has suffered a compression fracture of the vertebræ when continuation of treatment is strongly indicated. There is no reference to electronarcosis, which is finding favour amongst a small number of psychiatrists. The term "epilepsies" has replaced "cerebral dysrhythmias" in chapter four, which has been rewritten. Dr. Hill maintains that alkalosis increases, while acidosis decreases, the inborn tendency to convulsions. There is a full discussion of emotional, physiological and biochemical factors, but observations to the effect that the tendency to fits was not increased during air raids seemed to discount fear, anxiety and anticipatory tension as relevant factors. On the other hand emotions such as frustration involving the adrenal-sympathetic systems tend to precipitate epileptic attacks. Chemotherapy does not exclude the recognition of personal and environmental factors which call for modification and adjustment. A chapter on the use of drugs in psychotherapy includes a section on "excitatory abreaction" with ether, of value for the unmasking of repressed material in the hysterical personality which has broken down under conditions of acute and exceptional stress. It may be mentioned at this point that the unusual stresses of war give rise to acute emotional reactions which bear a good prognosis when the patient is protected from further stress and that the practice of psychiatry under war conditions encourages a degree of optimism which subsequently is not supported by experience in ordinary peacetime civilian practice. In the section on prefrontal leucotomy the authors report that their earlier impressions have been confirmed of the good results of this operation in certain types of obsessionals who have not responded to electrical convulsion therapy and psychotherapy. In their opinion penicillin G, in amounts up to six or eight million units, is more effective when combined with malaria than either alone in the treatment of general paralysis. Papers are, however, coming forward with evidence that penicillin alone is an effective therapeutic agent and even to be preferred to malaria.

This is a stimulating work and indispensable for the psychiatrist in general and special hospital practice. The authors deal essentially with the application of physical methods in psychiatry and are careful to avoid creating the impression that psychotherapy is superseded. It is of some interest to note that in the Mill Hill War Emergency Hospital for psychoneurotic casualties, where both authors worked on a series of over 7000 male and female patients, only some 15% received systematic physical treatments, while 90% received in addition or exclusively psychotherapy by discussion and reeducation.

[1] "An Introduction to Physical Methods of Treatment in Psychiatry", by William Sargant, M.A., M.B. (Cantab.), M.R.C.P., D.P.M., and Eliot Slater, M.A., M.D. (Cantab.), F.R.C.P., D.P.M., with a chapter on treatment of the epilepsies by Denis Hill, M.B. (London), M.R.C.P., D.P.M.; Second Edition; 1948. Edinburgh: E. and S. Livingstone, Limited. 8½" × 5½", pp. 232. Price: 10s. 6d.

HUMAN NUTRITION.

THERE are not many works upon medical subjects which can hold the attention of a reviewer as easily as "Human Nutrition", by V. H. Mottram, who was formerly Professor of Physiology at King's College, University of London.[1] This book contains a complete survey of all aspects of nutrition and the author is to be commended for presenting his subject in such an interesting and entertaining manner. Well-balanced common sense dictates the treatment of many topics; thus routine purgation is severely criticized, but when discussing drinking with meals the author states: "It looks as if the ordinary person may as well drink with meals. After all he has done so for some thousand or more years without dire results." A tolerant viewpoint is shown towards alcohol, but at the same time it is deplored that, in a world short of food, such a percentage of the food values of cereals, grapes, apple juice *et cetera* is wasted "in order to make expensive beverages of a doubtful dietetic value, however pleasant they may be". The author agrees that there are very many different ways of obtaining an optimal diet, and he cites George Bernard Shaw as a good example of a man able to thrive mentally and physically despite an absence of meat in his diet.

In a discussion on the subject of food hygiene in the home it is practically stated that "the biggest reform necessary in the British kitchen is the installation of a refrigerator"—a fact which applies even more to this country. This book will prove a most useful addition to every doctor's bookshelf.

A TEXT-BOOK OF PUBLIC HEALTH.

DESIGNED as a text-book for medical graduates studying for the Diploma of Public Health, "Frazer and Stallybrass" is admirably suited to the purpose. The appearance of a twelfth edition so soon after its predecessor (the eleventh edition was published early in 1946 and is now out of print) is an indication of its popularity among those for whom it was printed.[2] There are, however, all too few candidates for the diploma in Australia, but there is a large class of medical practitioners to whom the work should appeal, namely, the part-time medical officers of health. To those who need an up-to-date work of reference on public hygiene and social medicine the volume can be confidently recommended.

Into its 570 pages is packed a wealth of information. It is true that nearly half of its contents relate to British health laws and administration, and that there has been but little change in the purely scientific parts of the book, but the chapters on environmental sanitation are very complete, and well illustrated, as are those on the infective diseases and epidemiology.

It is, however, in the chapters on health law and administration that there has been most change. Recent developments in social medicine in the Old Country have rendered

[1] "Human Nutrition", by V. H. Mottram, M.A. (Cantab.); 1948. London: Edward Arnold and Company. 7½" × 4¾", pp. 160. Price: 6s. 6d.

[2] "Text-book of Public Health" (Formerly Hope and Stallybrass), by W. M. Frazer, O.B.E., M.D., Ch.B., M.Sc., D.P.H., and C. O. Stallybrass, M.D. (State Medicine), Ch.B., D.P.H., M.R.C.S., L.R.C.P., Order of St. Sava; Twelfth Edition; 1948. Edinburgh: E. and S. Livingstone, Limited. 8½" × 5¾", pp. 582, with many illustrations, some of them coloured. Price: 30s.

necessary a complete revision of these. Although the details do not apply to this country, they will repay study. A knowledge of the application of the principles of social medicine in Britain is well worth acquiring in view of recent legislative trends in Australia. The final chapter on "Social Services" is of particular interest in this respect, containing as it does a brief abstract of the Beveridge Report.

The book is particularly well indexed and well illustrated, and the type is clear.

GYNÆCOLOGICAL AND OBSTETRICAL ANATOMY.

"GYNÆCOLOGICAL AND OBSTETRICAL ANATOMY" by C. F. V. Smout and F. Jacoby, the first edition of which was written by Smout and published under the title of "The Anatomy of the Female Pelvis", is a comprehensive work on the subject and is very well and clearly illustrated.[1] Many chapters are valuable contributions and should be helpful to undergraduate and graduate. The first five chapters are good solid anatomy. The chapters on the ovary and its development and ovarian endocrine function are up to date and give a clear view of the subject. The chapter on the uterus and vagina and that on the genito-urinary tract might have given a greater amount of attention to the vascular supply of the pelvis, which from the gynæcologist's point of view is treated very lightly. The origin and relations of the uterine, superior vesical and inferior vesical arteries might have been given far more prominence. The chapters on lymphatic drainage and innervation of the pelvic viscera are quite complete.

It is questionable whether the chapter on the placenta and that on the anatomy of the fœtus in relation to childbirth should be given so much prominence in a book of this type when these subjects are considered in most obstetrical text-books. If they have a place here they are very good, especially the chapter on the placenta with its diagrams, pictures and photomicrographs.

It is felt that a smaller more truly anatomical book would have a greater distribution amongst practitioners, as some of this work is a duplication of parts of books on obstetrics.

TREATMENT OF COMMON SKIN DISORDERS.

THE third edition of Sulzberger and Wolf's "Dermatologic Therapy in General Practice" has been revised and reset, but changes have been kept to a minimum consistent with bringing the book entirely up to date.[2] New subject matter includes modern views on the use of antibiotics and chemotherapy, and high-dosage calciferol therapy. As in previous editions of the book discussion is limited to the common dermatoses, and details of such "specialist" procedures as X-ray therapy are omitted, the authors being thus allowed to give a much more detailed account of the management of the common skin disorders than one finds in the ordinary text-book.

The chapter on "Principles of Topical Medication" is one of the best in the book. The factors to be considered in the choice of local remedies, of the vehicle to be used, and of the method of application and removal are discussed at length. The wisdom of using only few remedies and being thoroughly conversant with their properties is emphasized. It is unfortunate that in some of the following chapters many different remedies are enumerated, without a decided expression of the authors' opinion as to their relative efficacy in the disease under consideration.

Of the newer ideas included in the book, especially worthy of mention is the view that the possibility of sensitization to penicillin by its local application should interdict its use in this manner except for pyodermata which have proved unresponsive to older and more trustworthy remedies.

This book should undoubtedly maintain its previous popularity, and prove of great practical value to the student and the general practitioner.

[1] "Gynæcological and Obstetrical Anatomy", by C. F. V. Smout, M.D., M.R.C.S., with chapters on The History of the Female Reproductive Tract and its Endocrine Control by F. Jacoby, M.D., Ph.D.; Second Edition; 1948. London: Edward Arnold and Company. 8½" × 5½", pp. 260, with many illustrations, some of them coloured. Price: 40s.

[2] "Dermatologic Therapy in General Practice", by Marion B. Sulzberger, M.D., and Jack Wolf, M.D.; Third Edition; 1948. Chicago: The Year Book Publishers Incorporated. 8" × 5½", pp. 688, with many illustrations. Price: $7.75.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Malignant Disease and its Treatment by Radium", by Sir Stanford Cade, K.B.E., C.B., F.R.C.S., M.R.C.P., with a foreword by Sir Ernest Rock Carling, F.R.C.P., F.R.C.S., F.F.R.; Volume I; Second Edition; 1948. Bristol: John Wright and Sons, Limited. 9¾" × 6½", pp. 396, with illustrations, some of them coloured. Price: 52s. 6d.

The first volume of a completely revised edition of an authoritative work; it is being issued in four volumes.

"The Medical Clinics of North America" (issued every two months); 1948. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. Mayo Clinic Number. 9" × 6", pp. 371, with illustrations. Price: £5 5s. (paper binding) and £6 6s. (cloth binding) per clinic year.

Contains a symposium on anomalies of the heart and other miscellaneous papers.

"The Surgical Clinics of North America" (issued every two months); 1948. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. Lahey Clinic Number. 9" × 6", pp. 286, with illustrations. Price: £5 5s (paper binding) and £6 6s. (cloth binding) per clinic year.

Consists mainly of a symposium on diseases of the spleen, biliary tract, liver and pancreas, with papers on a number of other miscellaneous subjects.

"Medicine and Science in Postage Stamps", by W. J. Bishop, F.L.A., and N. M. Matheson, F.R.C.S.; 1948. London: Harvey and Blythe, Limited. Distributors: H. K. Lewis and Company, Limited. 7½" × 4", pp. 86, with illustrations. Price: 7s. 6d.

Deals with the story behind postage stamps of medical and scientific interest rather than with the purely philatelic details.

"Sex Variants: A Study of Homosexual Patterns", by George W. Henry, M.D., with sections contributed by Specialists in Particular Fields, sponsored by Committee for the Study of Sex Variants, Incorporated. One-Volume Edition; 1948. London and New York: Paul B. Hoeber, Incorporated. 9" × 6", pp. 1156, with illustrations. Price: $8.00.

The author has endeavoured to give an accurate report of the lives of eighty sex variants, without personal bias or theoretical assumptions.

"Progress in Neurology and Psychiatry: An Annual Review", edited by E. A. Spiegel, M.D.; Volume III; 1948. New York: Grune and Stratton. 9" × 6", pp. 678. Price: $10.00.

A survey of the significant literature of the previous year.

"The Leptospiroses", by P. H. Van Thiel; 1948. Leiden: Universitaire Pers Leiden. 9" × 6", pp. 246, with illustrations. Price: f.16.50.

A survey of the leptospiroses and the literature on their investigation.

"Handbook of Parentcraft", by Leslie George Housden, O.B.E., M.D.; 1948. London: Eyre and Spottiswoode. 7" × 4¾" pp. 152. Price: 5s.

Talks to young women, whether they are married or about to marry or just have the care of young children.

"Royal Melbourne Hospital Clinical Reports: Centenary Volume, August, 1948", edited by A. J. M. Sinclair; Melbourne: Royal Melbourne Hospital Old Students' Association. 9½" × 7", pp. 319, with illustrations. Price: 21s.

A representative collection of the formal addresses delivered at the scientific sessions of the Royal Melbourne Hospital centenary celebrations.

"Principles Governing Eye Operating Room Procedures", by Emma I. Clevenger, R.N.; 1948. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9½" × 6", pp. 218, with illustrations. Price: 41s.

A manual for nurses and doctors concerned in the preparation of eye operating theatres.

"Practice of Allergy", by Warren T. Vaughan, M.D., revised by J. Harvey Black, M.D.; Secand Edition; 1948. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" × 6½", pp. 1156, with illustrations. Price: £5 12s. 6d.

A comprehensive consideration of allergy.

"Handbook of Ophthalmology", by Everett L. Goar, A.B., M.D., F.A.C.S.; 1948. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9¾" × 6½", pp. 170, with illustrations, some of which are coloured. Price: 41s.

Written primarily for medical students.

The Medical Journal of Australia

SATURDAY, OCTOBER 30, 1948.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

VETERINARY MEDICINE.

THE medical care of animals for long lagged behind after human medicine had begun to discard the superstition and unfounded empiricism of a less critical age, and many people even today are not aware of the great strides that have been made in veterinary medicine, strides that have brought it up to a respected place beside human medicine in scientific thought. W. I. B. Beveridge, a graduate in veterinary science of the University of Sydney, was recently appointed to the chair of animal pathology in the University of Cambridge, an appointment which, as Professor Beveridge pointed out in his inaugural lecture,[1] is a tribute to Australian science, and more particularly to Australian veterinary science. In his lecture Beveridge has brought forward many interesting facts and comments concerning veterinary medicine and its teaching which should be of interest to followers of medical science. He discusses the important role of animals in providing for man's needs since very early times and the gradual domestication of animals: first the dog, then the ox, the ass, the buffalo, the sheep, the goat and the pig; later came geese, ducks, pigeons, cranes, cats and antelopes (in Egypt), camels (in Arabia) and horses which were introduced from Persia to Mesopotamia, under the name "ass of the East" (the camel was called "ass of the South"), soon after 2000 B.C. and into Egypt and Syria about 1000 B.C. Veterinary practice was mentioned in the code of Hammurabi (*circa* 1800 B.C.) and became highly developed in the Byzantine Empire where the veterinary equivalent of Hippocrates, who was named Apsyrtus, was born about A.D. 330. Veterinary medicine was quite neglected in mediæval Europe, only the Arabs, "who valued their horses above their women", keeping it alive, and it remained at a low ebb until the latter part of the eighteenth century. The first European veterinary college was established in France at Lyons in 1763, and by the end of the century colleges were established in all the leading European countries, 21 in all, including the first British school in London in 1792. However, the handling of animals, especially dead animals, still brought a certain stigma on the students, and it took another century for the profession to achieve worthwhile status. Unfortunately the London college which started well (much assisted by the great John Hunter) fell into wrong hands and the ground lost was not quickly regained. In 1881 a law was passed in England forbidding the use of the title veterinary surgeon except by persons properly qualified, and, as Beveridge puts it, "at least among livestock owners and in scientific circles, the veterinarian is now esteemed as highly as graduates in any other branch of science". The achievements of veterinary medicine in preventive measures against animal disease, for example, by prophylactic vaccination, are impressive; in research they compare favourably with those of the medical profession.

At present, according to Beveridge, there are five veterinary colleges in the British Isles, ten in the United States of America, three in France, two in Belgium and Canada, one in Holland, Denmark, Norway, Sweden, Australia and South Africa; there were five in Germany before the war. The course lasts mostly five years, occasionally six years, and runs parallel to the usual medical course: the basic sciences are studied in first year, anatomy and physiology in second and third year with pharmacology and related subjects, nutrition and animal husbandry, genetics (including practical breeding) and hygiene. In fourth year clinical work is started with pathology, bacteriology, immunology, protozoology and parasitology, and fifth year is occupied with medicine, surgery and obstetrics together with meat inspection and veterinary jurisprudence. In some countries, including Australia, a period of practical experience on a farm is required. All schools have hospitals attached and some have animal husbandry farms. The animals studied include the horse, ox, sheep, goat, pig, dog, cat and poultry with the camel and elephant in countries where they are used, the honeybee on the Continent, fish in France and fur-bearing animals in the United States. The day of the horse having passed, farm animals are the most important subjects of veterinary practice today. In conformity with this, the present emphasis, according to Beveridge, is towards considering the herd rather than the individual (an interesting development in the light of certain modern human ideologies) and towards the prevention rather than the treatment of disease.

Commenting on the curriculum, Beveridge points out that the basic sciences and most of the physiology and biochemistry are the same as that taught to medical students; the anatomy of the dog which he favours as the basis of veterinary anatomy is not greatly different from that of man; the general principles of pathology, bacteriology and immunology are the same in human and veterinary medicine and on the research level there is no distinction at all; the study of animal infectious diseases is heavier than the human subject because of their greater number; the study of bacteriology in a veterinary school is, if anything, more extensive than in a medical school, and parasitology and protozoology are much larger subjects, at any rate in non-tropical countries; veterinary clinical medicine and surgery are "sciences and arts in their own right". In addition there are the specific veterinary subjects, animal management, hus-

[1] "Veterinary Education: An Inaugural Lecture", by W. I. B. Beveridge; 1948. Cambridge: Cambridge University Press. 7¼" × 4¾", pp. 40. Price: 1s. 6d.

bandry, production, hygiene, nutrition and breeding, sometimes included in a general name such as zootechny or animal husbandry.

Professor Beveridge then goes on to discuss the proposed course in veterinary science which it is hoped soon to establish at Cambridge, making a special plea for the encouragement of research. His own attitude is the scientific one that looks beyond a narrow field to all related fields of knowledge and research, and he sees in Cambridge the ideal place for the development of collaboration between veterinarians and other scientists, particularly medical and agricultural scientists, and for the veterinary student to obtain a broad and fundamental education. Professor Beveridge has a stimulating approach and a wide vision; his lecture will interest most people, but should especially be read by any who have not yet realized that veterinary medicine has not only come of age, but has attained full manhood. In one respect the State, in New South Wales at least, has shown its concern for animal health and its confidence in the knowledge and judgement of its qualified veterinary practitioners. It is an offence for a person not registered as a veterinary practitioner to treat diseased animals for gain. On the other hand anyone, even knave or fool, may treat a sick person and charge what he will for so doing.

Current Comment.

HISTOPLASMOSIS.

SINCE Darling in 1905 found the microorganism which he named *Histoplasma capsulatum* in the tissues of a patient dying of disease resembling kala-azar, less than 100 cases of histoplasmosis have been reported. The first case to be placed on record in Australia is reported in this issue by D. W. Johnson and E. H. Derrick, of Brisbane, who have also presented a summary of the main features of the disease. It has been customary to regard histoplasmosis as characteristically rare and almost uniformly fatal, but recent investigators have cast doubt on both these assumptions. Johnson and Derrick suggest in their paper that histoplasmosis may repeat the history of many diseases that were at first known only from fatal cases and mention that several authors have postulated a subclinical grade of infection to explain the large number of reactors to the histoplasmin test who appear to be in good health. This is given further support by a recent report by I. L. Bunnell and M. L. Furcolow[1] of ten proved cases of histoplasmosis all occurring in the Kansas City area within a period of nine months. The patients were culled from a large group of school children, hospital patients and patients referred for consultation by private practitioners and were subjected to an exhaustive series of investigations of both positive and negative significance. In nine cases the diagnosis was confirmed by the isolation of *Histoplasma capsulatum* from cultures, and in one by the typical microscopic appearance of intracellular parasites. In each case the diagnosis was substantiated by more than one laboratory test. In four cases the organism was isolated from the patient's gastric contents, an occurrence which, according to these investigations, has not been previously reported. All of the patients lived within a radius of 200 miles of Kansas City, which bears out the assertion that whenever intensive search for the disease has been made, an appreciable increase in the number of reported cases has resulted; its rarity may be as much related to diagnosis as to incidence. With regard to the gloomy prognosis, it is worth noting that of the ten patients in this group five were still alive when the report was written; two had apparently recovered completely (apparently without specific therapy), a third was expected to recover and the prognosis for the other two was doubtful. Of those who died the cause of death in one case was not histoplasmosis but surgical shock. Bunnell and Furcolow draw attention also to another interesting feature, the presence (as shown by X-ray examination) in the lungs of one of those who recovered of miliary lesions which were observed to be healing by calcification. He has been followed for three years, during which he has been well enough to attend school, and definite deposition of calcium in the lesions has been observed. This supports the suggestion of other workers, based on histoplasmin skin testing and X-ray finding, that there exists a benign form of histoplasmosis whose final stage is represented by pulmonary calcification. It seems likely that reports of this disease will become more frequent and with the accumulation of data light may be thrown on the assessment of prognosis. The report of Johnson and Derrick should arouse awareness of the disease in Australia and further reports will be awaited.

[1] *Public Health Reports*, March 5, 1948.

PSYCHIATRY IN ENGLAND.

PSYCHIATRY has come more and more into prominence as our progressive civilization has elaborated and refined its methods of warfare, and it must be admitted that a good deal has been learnt through the unhappy medium of war. An illuminating account of psychiatry in England during the years of the second World War has been recently given by William Sargant,[1] who regards the Battle of Britain and Dunkirk as psychiatric milestones. Prior to that period there was doctrinaire psychotherapy at neurosis centres. The arrival of men suffering from severe war shock and a genuine fatigue state based on overwork, sleeplessness and underfeeding led to the elaboration of a multidimensional approach. Efficient sedation, sleep therapy, modified insulin treatment and barbiturate abreaction commenced to be used as a more complete and all-round approach to treatment. As Sargant says:

> I believe that enormous sums of money have been saved the British and American governments in pensions because Dunkirk came to our rescue in time and again reminded us of an important fact—that the brain and the body must often be treated on the same sort of basic principles. It is just as important, for instance, to splint the nervous system, recently shattered by bombing, with heavy sedation as it is to splint the broken limb until both can be reset. Psychotherapy was not found half so effective when a patient was still 20 pounds below his normal weight as when that weight was also restored by a suitable physical treatment, such as modified insulin.

With these changes of attitude the psychiatrist himself progressed. Before the war he had tended to be too conscious of his speciality; later he became both psychiatrist and physician. Many points on treatment are mentioned by Sargant. He explains that the method of drug abreaction as devised by Slater and himself was accidentally discovered in the use of "Sodium Amytal" as a sedative. It is now realized that the agent employed should be graded to the task in hand. With this method there is considerable variation in results, and individual patients may respond to "Sodium Amytal", "Pentothal", ether, ether and barbiturates, or "Methedrine". He points out the individuality of the psychiatric approach; there being now no universal cure-all-therapy, the approach is based on personal experience and past treatment observations. "The right selection of cases for a particular treatment emerges from careful clinical analysis and observation of each case." As an example, electroshock may make persons with a depersonalization syndrome worse, but they improve considerably under ether abreaction with the production of an intense excitement. Although physical therapy plays a large part in the attack on mental disease there is still scope for psychotherapy; group psychotherapy

[1] *The Journal of Nervous and Mental Disease*, June, 1948.

techniques, including psychodrama and the like, are important. The problem of schizophrenia has not been solved; insulin or combined insulin-electroshock is the best form of treatment so far devised. Lobotomy gives good results particularly in well-integrated obsessionals; as an example, one leucotomized patient looks after a husband and seven children in addition to an outside job. To sum up the treatment position there are now few patients for whom we can do nothing, and Sargant believes that the next few years will see equally startling advances; we have hardly crossed the frontier of treatment. Concerning rehabilitation, comment is made on the tendency to over-emphasize the ancillary aids. If a patient is cured, he can usually "stand on his own feet, attend ordinary training centres and needs no special concessions". In a consideration of the psychiatrist's position, Sargant, as a result of his experience, concurs in the famous dictum of Weir Mitchell:

> You are labelled as medical superintendents and some of you allow your managers to think that you can be farmers, stewards, caterers, treasurers, business managers and physicians. Knowing what we do about the rate and growth of medicine, does any man in his senses think he can be decently competent? Insist to your managers that you are physicians and no more.

He deplores the incursion of psychiatry into psychosomatic medicine, selection of personnel and advising on morale, marriage, industry and the prevention of wars. He pleads for clinical research and more clinical research at the bedside. "We must learn the right treatment of the right patient at the right time and by the right combination of methods." No one will deny that the author's methods pay handsome dividends in individual therapy. It will be remembered, however, that he has achieved his pre-eminence as a clinician in a hospital and that this is his sphere rather than field work in mental and social hygiene which he has left to others.

PENICILLIN IN DIPHTHERIA.

THOUGH the value of penicillin in the treatment of diphtheria has been known from its early days to be considerable there is still uncertainty as to its degree. Fortunately clinical material is not abundant for such studies, and the dangers of *gravis* infections and the importance of trying to avoid carrier states are such that the attitude of physicians is naturally one of caution. An interesting study has been published on the results of the treatment of naso-pharyngeal diphtheria by penicillin. In this Edward W. Bixby recounts his results obtained in treating 139 young men in the United States occupation forces in Germany over a period of eight months.[1] All these patients suffered from proven diphtheria affecting the naso-pharynx, and virulence of the isolated organisms was established in every instance. Eighty-eight men were treated with the usual medical methods of bed rest and local washes and gargles and 100,000 units of diphtheria antitoxin given intramuscularly immediately the bacteriological diagnosis was made. As most of the patients had the usual initial symptoms of sore throat they had received also sulphadiazine until the exact diagnosis was established. The remaining 51 patients received in addition one million units of penicillin, given in 50 doses of 20,000 units every three hours. Cultures from the nose and throat were made after the first fortnight, and again two weeks later. If no organisms were grown a further series of cultures were made at intervals of two days to make sure that the patient was not a carrier. If, however, the organisms of diphtheria appeared on any culture after the first it was found that this indicated the beginning of a chronic carrier state in 90% of cases. The culture made at the end of a fortnight was particularly useful in this regard. Of the men treated by the "routine" method of antitoxin forty yielded a positive culture only after this interval of a fortnight, and these then received a course of penicillin. This series thus constituted a "late penicillin" group, which could be contrasted with the "early" group. A few patients received a second course of penicillin, but even this did not affect their carrier state, for which tonsillectomy alone was effective. The most important difference between the two series was the effect of the early administration of penicillin in preventing the carrier state. The comparative figures showed that 79% of the early series lost all bacteriological evidence of their infection within two weeks, but in the late series only 31%. In other words, not only was the period of hospital treatment lowered by the early administration of penicillin, but the incidence of carriers was also reduced. It is interesting that in the first few months of this investigation the majority of the infections were by the *gravis* type of organism. During the later period the *mitis* type replaced the other, but there was no significant difference in the incidence of complications in either group. Complications of a serious kind were not seen in any patient of the whole series. No significant difference in the appearance of electrocardiographic abnormalities could be traced in the different categories of patients, but there was a suggestion that the longer the organism remains in the throat, the greater the chance of carditis, at least of the grade which can be recognized only by the electrocardiograph. Lastly, it is interesting to read that all these men had been previously immunized by the standard army procedure, but no information was given concerning the dates of completion of the injections or of "boosters". The collection of a series like this is of real value, especially as it deals with a form of diphtheria which is insidious and of great importance to the public health.

Some other aspects of the use of penicillin in diphtheria are considered in a recent British report.[1] A subcommittee of the Public Health Laboratory Service investigated the penicillin-sensitivity of 284 strains of *Corynebacterium diphtheriæ* isolated in different parts of the country and found that most of the strains were two or three times as resistant to penicillin as the Oxford staphylococcus. *Gravis* strains were more resistant than *intermedius*, and *intermedius* were more resistant than *mitis* types. The results, however, make it clear that strains of *Corynebacterium diphtheriæ* of all three types tested were sensitive *in vitro* to concentrations of penicillin which can readily be reached in the body. The subcommittee also investigated the capacity of penicillin to clear throats of the organism. Among 65 patients with acute faucial diphtheria treated with penicillin, 26 of 37 receiving a three-day course, and 23 of 28 receiving a six-day course, became free of the infecting organisms within four days of the end of treatment. The series included a proportion of immunized subjects, but there was no evidence that immunization affected the clearance rate. The response among carriers was more disappointing, though the number treated was too small to allow definite conclusions to be drawn. Among 31 persistent diphtheria carriers treatment with penicillin was followed by rapid disappearance of the organisms in only 13 cases and possibly in some of these the throat would have become clear spontaneously during the test. The subcommittee suggests that it may well be easier to prevent with penicillin the subject of the acute infection from becoming a convalescent carrier than to cure the established carrier condition. If this is so, there is every reason to begin penicillin therapy as early in the disease as possible and not to wait until the diphtheria organism has become firmly established in diseased tonsils.

[1] *The American Journal of the Medical Sciences*, May, 1948.

[1] *The Lancet*, October 2, 1948.

INDEX TO "THE MEDICAL JOURNAL OF AUSTRALIA".

THE index to THE MEDICAL JOURNAL OF AUSTRALIA for the half-year ending June 30, 1948, has been published. Copies will be sent as usual to those on the regular index mailing list. Readers who wish to receive a copy of the index and who have not asked to have their names placed on the list are invited to communicate with the manager at The Printing House, Seamer Street, Glebe, New South Wales.

Abstracts from Medical Literature.

RADIOLOGY.

Physiological Stasis.

ARTHUR A. BREWER (*American Journal of Roentgenology*, July, 1947) states that physiological stasis of the gall-bladder may occur when a patient has eaten no fats for a period of twenty-four hours or more. The gall-bladder is filled with a thick concentrated bile and fresh dye-laden bile is unable to enter. Physiological stasis should always be considered when evaluating non-visualization of the gall-bladder, and it is of even more importance when the shadows are faint. When there is a history of fat-free diet or vomiting and limited food intake prior to examination, a faint shadow is of indeterminate significance and non-visualization must be viewed with suspicion. Whenever possible the authors insist that the patient have a fatty meal at noon the day before examination; in addition to any food desired, he must take one pat of butter, one soft boiled egg, and one glass of half milk and half cream. It is obvious that the fat meal must be given early enough to complete its action before ingestion of the opaque medium.

The Differentiation of Patent Ductus Arteriosus and Atrial Septal Defect.

A. D. NICHOL AND DON D. BRANNAN (*American Journal of Roentgenology*, December, 1947) state that patent *ductus arteriosus* and atrial septal defect can be differentiated by their clinical and radiological features. In patent *ductus arteriosus*, blood from the aorta, the highest mean pressure point of the circulatory system, is shunted to the pulmonary artery, already filled with blood. The pulmonary artery dilates to accommodate this increased volume which, on returning to the heart, causes enlargement of the left atrium. The increased filling of the left atrium, and of the left ventricle, increases the systolic output delivered to the aorta. Even though a considerable part of the left ventricular output is shunted through the ductus, the peripheral flow is usually only slightly decreased. The shunt occurs between high pressure vessels, but the pressure differential is sufficiently high to cause blood to flow through the ductus only from the aorta to the pulmonary artery. The authors have never seen cyanosis which could be attributed with certainty to a reflux of venous blood through an uncomplicated patent ductus. In atrial septal defect, the right atrium receives the peripheral venous flow and apparently, in numerous instances, a large complement of blood from the left atrium. This increased volume of blood causes great enlargement of the right atrium and right ventricle; it increases right ventricular systolic output which results in considerable enlargement of the entire pulmonary vascular system. When this increased blood volume is returned to the left side of the heart, the interatrial septal defect provides an escape mechanism which prevents an otherwise extreme enlargement of the left atrium, but the run-off through the septal defect also decreases left ventricular filling. This decreased filling results in decreased left ventricular output and decreased peripheral blood flow. It is probable that slight pressure changes will cause a reversal of flow; venous blood will enter the left side of the heart and be delivered to the peripheral circulation. Careful observation or an adequate history will occasionally elicit evidence of transient slight cyanosis in infants with an interatrial septal defect. In patent *ductus arteriosus*, the authors have been impressed with the absence of cyanosis, the prominent thrill and the characteristic murmurs, the essentially normal electrocardiogram with normal sinus rhythm, and on X-ray study, the large heart with the unusual combination of occasional slight enlargement of the left atrium and definite enlargement of the left ventricle, pulmonary artery and first and second portions of the aorta. The latter findings are believed to be responsible for some of the respiratory difficulties of infants with a patent ductus. The increased blood volume and the re-circulation through three large vessels (aorta, pulmonary artery and patent *ductus arteriosus*) creates an unusual mass of great vessels. The slightly large left atrium presses the tracheal bifurcation from below in a cephalad direction; a large ductus and large pulmonary arteries exert pressure posteriorly and medially to the right; the large first and second portions of the aorta have a similar tendency. As a result, tracheal deviation with compression and partial obstruction, particularly of the left main branch, occurs. In some infants, such an obstruction is a factor in the frequency, persistence and severity of pulmonary infections, and the obstruction may be a cause for retardation of development in infancy. As the child grows and the tracheal bifurcation descends, relatively more space is available for upper mediastinal structures and partial tracheal obstruction is spontaneously relieved. In atrial septal defect the impressive features are the variability of murmurs and thrills, the right axis deviation and the abnormal *P* waves of the electrocardiogram which may also show an unstable cardiac conduction mechanism. The X-ray findings are of paramount importance because of the characteristic increase in the size of the heart due to the great increase in the size of the right atrium and ventricle. The dilatation of the pulmonary artery and its branches or the dilatation of the conus is a constant finding. In contrast, the aortic knob is small and inconspicuous.

Some Experiences with Bone Tumours.

JAMES F. BRAILSFORD (*The British Journal of Radiology*, April, 1947) states that the latent period in malignant metastases to the skeleton may extend into many months. Because the initial radiographs taken to reveal the cause of pain failed to show any abnormality or sign of disease, the possibility that the cause may be secondary carcinoma must always be remembered in any person past middle life, and periodic X-ray examinations should be made if the symptoms persist. It is particularly important to repeat the examination if any manipulation under anæsthesia is contemplated, for such treatment may produce a fracture. Though it is always wise to consider the possibility that a lesion in a patient over thirty years of age is not primary, but a secondary metastasis from a distant site, and to seek to discover other sites before any surgical attack is made, there is nothing to be gained for the patient in seeking to find, by extensive and perhaps exhausting investigations, a primary neoplasm when metastases are evident. The mere knowledge that metastases can produce similar radiographic appearances to primary lesions, and that even at autopsy it may be impossible to distinguish the primary lesion, should check the inquisitive. The author suggests to those concerned with the education and training of radiologists that the student be taught more extensive radiology in its application to clinical methods at the expense of the practically useless physics, which now engages far too much of his time. He considers that the radiologist ought to make himself so familiar with all the radiological features which are met with in all the specialities, that he can give expert advice to the specialist seeking it. He will be able to do this only if he is not compelled to waste time in acquiring non-essential facts. A better knowledge of clinical medicine is far more important than a smattering of physics, which he can safely leave to the physicist.

Metallic Foreign Bodies in Brain Abscess.

ERNEST H. WOOD, JUNIOR (*American Journal of Roentgenology*, January, 1948), states that in a high percentage of cases of gunshot wounds of the head it is not easy to decide when a metallic foreign body retained in the brain should be removed and when it should not. It has been the general policy among neurosurgeons to remove those which are large and those which are easily accessible at the time of primary *débridement*. In other instances it has been believed that more harm would be done to the patient by the operative trauma of removing the fragment than by allowing it to remain in its place of lodging. In a fairly large number of cases in which metallic fragments were not removed a brain abscess has developed around the foreign body. This occurs more frequently during the early weeks following injury than during later months and years. The clinical signs of brain abscess secondary to a head injury are not always outstanding. Any finding which might lead to earlier diagnosis and treatment in these cases would appear to be of value. It has been found in this group of cases that gravitational movement of a metallic fragment in an abscess cavity may be demonstrated radiologically by examining the patient in both the horizontal and upright positions. The movement of a foreign body during the interval between two X-ray examinations also has been found to be associated with abscess formation. Metallic foreign body movement has been demonstrated so frequently in the group of penetrating brain wounds studied that it is believed that in all cases in which intracranial metallic fragments are not removed at the time of primary *débridement* the patient should be re-examined radiographically at some time within the first two or three weeks following injury. Radiograms should be taken in both the horizontal and erect positions at each examination.

These radiograms should also be compared carefully with any earlier films which are available for the detection of any change in position of retained metallic fragments. The development of symptoms suggesting an intracranial infection in association with a metallic foreign body is an indication for X-ray examination in the erect and horizontal positions.

"Neurotrophic" Lesions of Bone.

J. R. Hodgson, D. G. Pugh and H. H. Young (*Radiology*, January, 1948) state that lesions of the bones of the feet which have been described by certain writers as "neurotrophic" may be produced by a wide variety of systemic and local diseases. A review of 61 cases in which the radiograms of the feet presented evidence of such "neurotrophic change" revealed that in every case there was infection of contiguous soft tissue, while diseases of the nervous system were present in only a small proportion. It is believed, therefore, that the assumption that these bony changes are due to neurotrophic disturbance is invalid, and that they are rather to be attributed to a type of osteomyelitis secondary to chronic infection of the contiguous soft tissues. The process of osteoporosis and absorption may continue until the bone is entirely gone. If, however, the inflammatory process is checked for some reason at any point in the progress of the disease, there may be no further destruction. Thus, since the lesion may be halted at any point in its progress, radiograms may be obtained showing any stage of the process, and varying degrees of absorption and destruction may be demonstrated. Depending on the extent of the infection, a variable number of metatarsal bones or phalanges may be involved. The extent of involvement depends on how extensive the infection is, how good the blood supply to the extremity happens to be, how long the infection has been present, how much general resistance to the infection the patient may present, and many other possible complicating factors. The extent of the infection and its duration are of the chief significance.

Bagasse Disease of the Lungs.

D. V. LeMone, W. G. Scott, S. Moore and A. L. Koven (*Radiology*, November, 1947) state that inhalation of bagasse dust, derived from sugar cane after it has been crushed and the juice extracted, incites a pathological process in the lungs which has been termed "bagasse disease of the lungs" or "bagassosis". Information concerning bagassosis should be disseminated because bagasse is being used more extensively in the manufacture of thermal and noise-insulating building materials and in the manufacture of refractory brick. As such, it constitutes a serious industrial hazard unless properly handled. Pulmonary changes incited by the inhalation of bagasse dust consist in a diffuse infiltration and consolidation, an acute bronchiolitis or pneumonia, that is similar to that seen in pneumoconiosis, but in one respect it is greatly different. It is a reversible reaction, with the process undergoing resolution and the lung regaining its normal appearance on the radiogram. Whether or not the pathological reaction is due to fungi, bacteria, or a virus associated with the dust, or to an allergic response to the bagasse or its possible infectious agents or their products, or to some chemical or physical property of the dust, or to any combination of the above, has not been determined and is still open for investigation.

PHYSICAL THERAPY.

High Voltage X-Ray Therapy for Amenorrhœa and Sterility.

Ira I. Kaplan (*American Journal of Roentgenology*, March, 1948) discusses the treatment of amenorrhœa and sterility in women with high voltage X-ray therapy. The patients are divided into two groups: unmarried patients who complain of amenorrhœa and married patients whose complaint is of sterility and amenorrhœa or sterility alone. In all cases the patients had been referred by a physician or gynæcologist and in practically all cases every other method of treatment had been used first. The author points out that amenorrhœa is due to many causes; when the cause is congenital or pathological malformation, irradiation is useless, but it is of great value when the amenorrhœa is the result of physiological dysfunction. The action of X rays is discussed, in relation to whether they have a general stimulating effect, whether they cause the destruction of a persistent follicle which has failed to rupture or whether the effect may be on small ovarian cysts. The evidence so far is inconclusive. It is noted that about 7% of cases of sterility are due to pituitary dysfunction. The author has a series of 338 patients treated over a period of twenty-one years; of these 33 were unmarried and 305 married women. The method of treatment was as follows. On the first day 50*r* were given to the anterior right and left ovarian fields and 75*r* to the anterior pituitary area. One week later 75*r* were given to the anterior pituitary area and 75*r* to the posterior right and left ovarian fields. One week later the right and left anterior ovarian fields were given 50*r* and the anterior pituitary field 75*r* (all doses measured in air). Factors used were 200 kilovolts with filters of copper of 0·5 millimetre thickness and aluminium of 1·0 millimetre thickness. Only two patients received more than one course of treatment. Of the 334 patients who completed treatment 274 were followed up; favourable results were obtained in 210, 12 being unmarried and 198 married. Of the 198 married women, 90 became pregnant and went to term delivering 101 normal children. There were 32 additional pregnancies resulting in stillbirths, miscarriages or death of the child shortly after birth. There was only one abnormal birth. The author considers from his experience that such small doses of X rays, properly administered, can harm neither the mother nor the offspring.

Urethane Therapy.

T. Leucutia (*American Journal of Roentgenology*, March, 1948) states that in 1925 it was noted that animals subjected to urethane anæsthesia showed changes in the lymphoid system similar to those following whole body irradiation and further that rats under urethane anæsthesia succumbed to sublethal doses of X rays. The effect is due to the growth inhibiting power of urethane which suppresses mitosis of the cells. In 1946 Edith Paterson *et alii* published results of the action of the drug on patients suffering from leuchæmia and other malignant lymphoid disease. In nineteen cases of myeloid leuchæmia there was a remarkable response with a quick drop in the white cell count and often a rise in the hæmoglobin value. The spleen regressed in size and the general condition improved. The amount of urethane given varied from 19 to 34 grammes, being the amount necessary to bring the number of white cells down to 20,000. In thirteen cases of lymphatic leuchæmia, improvement was less pronounced. There was no indication from the body weight or the rate of fall of the white cell count as to the final dosage necessary. Side effects were nausea in 50%, vomiting in 25% of cases. In a few instances the symptoms were severe enough to necessitate withdrawal of the drug. A study was also made of the effect of urethane, in thirteen cases of advanced carcinoma of the breast and in thirteen cases of other malignant disease. Transitory regression in size was obtained in seven cases only. The author has studied the remaining literature on urethane therapy and finds that there are no claims for permanent cure and that the drug is not without danger as aplastic anæmia may develop. It is also pointed out that urethane is a carcinogenic agent. It is concluded that urethane therapy is of limited value. In the leuchæmias it leads to palliation of variable duration, but repeated blood marrow examinations are necessary during the course of treatment. In malignant neoplasms its value is doubtful. If used for patients with an expected long survival time, the carcinogenic effect must be kept in mind.

Giant Follicular Lymphadenopathy.

Erich Uhlmann (*Radiology*, February, 1948) states that giant follicular lymphadenopathy (Brill-Symmers disease) is a disease of the lymph nodes which may be followed by or transformed into lymphatic leuchæmia, polymorphous cell sarcoma or Hodgkin's disease. The condition strongly resembles Hodgkin's disease and in most instances is diagnosed as such. Characteristically there is general or local enlargement of lymph glands often with splenomegaly. Usually the general condition is little affected. Histologically there is numerical and dimensional hyperplasia of the lymph follicles and frequently it is difficult to distinguish from the hyperplasia which occurs in inflammatory conditions. Chronic lymphadenitis and chronic lymphatic hyperplasia are frequent terms used by the pathologist to describe the findings. A series of 22 cases is reviewed. In fifteen cases the diagnosis has not changed, although nine of the patients in this group have been followed for less than three years. Three patients developed leuchæmia, one polymorphous cell sarcoma, one leucosarcomatosis and two Hodgkin's disease. Of the nine patients living three to nine years, eight received large amounts of radiation and the author concludes that this has caused their survival. Small amounts of radiation will cause disappearance of the nodes, but large doses are necessary for good results. The disease should be regarded as potentially malignant even in the early stages.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on May 27, 1948, at the Robert H. Todd Assembly Hall, British Medical Association House, 135, Macquarie Street, Sydney, COLONEL A. M. MCINTOSH, the President, in the chair.

The Surgical Treatment of Parkinson's Disease.

DR. W. LISTER REID read a paper entitled "Studies on the Tremor-Rigidity Syndrome: I. Surgical Treatment of Human Subjects". This article appeared in the issue of October 23, 1948, at page 481.

DR. V. J. MCGOVERN said that the disease which they had been investigating in dogs was a manifestation of encephalitis that frequently followed distemper, after periods of days, weeks, months or years. It was supposed to be due to distemper, but that question was under investigation. The dogs had various symptoms resembling those of humans. Six dogs were operated on in the acute phase of encephalitis; all of them died. Of the three dogs operated on which survived, two had become perfectly normal, and the third had a slight tremor after exercise. It was unfortunate that the university had holidays, because the dogs had had to be destroyed. The periods after operation on these three dogs were four months in two instances and two months in one, and the results were very good. In all three dogs the condition was presumed to result from infection and encephalitis was present. The pathological examination was interesting and useful as a study of encephalitis as a pathological process; but as a means of localizing the seat of the disease in humans it might be of use or it might not. There were only two sites in which lesions were common to all dogs; one was the cerebral cortex, the other was the cerebellum. There might have been lesions elsewhere that were not discovered. Of course, lesions due to encephalitis were also present. Dr. McGovern said that the work was still in progress. It was unfortunate that there were no photographs of the dogs that had been cured. There was one great difficulty. Dogs in the acute stage frequently died, or were taken to veterinary surgeons who destroyed them; there were very few in the chronic stage, and those were mostly kept by their owners. It was impossible to get dogs in the chronic phase.

DR. R. A. MONEY thanked Dr. Reid for his paper and congratulated him on its presentation and results. Dr. Money said that, like all other neurosurgeons, he had been worried by people suffering from Parkinson's disease who wanted to have something done for it. Most of the agitation seemed to have started from reports in the lay Press, especially in America, in which appeared glowing accounts of how these patients were being cured. He himself had been in two minds; he had not known whether to regard the supposed cure as being worthless, or whether there was anything in it. He was interested in watching Dr. Reid's work, but he was not yet convinced that the results were sufficiently good to justify his undertaking the procedure himself. However, something would have to be done, because Parkinson's disease was a far more distressing condition than many others on which much time and energy were spent. Most of the patients were nuisances to themselves and to their relatives. Unfortunately, they had their full mental faculties and realized their position only too well.

Dr. Money said that he had recently been abroad, and at every place which he had visited in Great Britain, on the Continent and in the United States of America he had tried to find out something of the treatment of Parkinson's disease. At all the recognized centres they had told him that it was still in the experimental stages. Even Professor Wilder Penfield said that he knew of no operative treatment and did not believe in the performance of any surgical procedure on the cortex. In Chicago all the authorities said that they had been unable to find any satisfactory treatment. The chief difficulty was that the condition had not been reproduced in animals; but during the week-end spent in Chicago Dr. Money had watched experimental work being done on monkeys, electrodes being placed in the vicinity of the *substantia nigra* to cause small areas of destruction there. He did not see the results, but he believed that there was one monkey which, if it lived, would develop Parkinsonism. Once the condition could be reproduced there might be a means of working out a cure. Referring to Klemme's work, Dr. Money said that the reports had been so unfavourable that he did not go to see him at St. Louis. He thought Dr. Reid might have something better than Klemme, because he could show some good results with regard to rigidity, which was the crippling factor.

Dr. Money said that many years earlier, with the late Professor F. P. Sandes and Dr. Eric Susman, he had had a patient with a localized tremor of one hand of unknown origin. At operation under local anæsthesia it was possible to stop the tremor by isolating the area of cortex from which it was arising and pressing on it with a finger; the result might possibly have had something to do with interference with the blood supply. They had even put in a piece of gauze to cause pressure on the selected area of cortex and left it for a week, the tremor being relieved for about six months; but it returned later. Another patient was in an advanced state of choreoathetosis due to a disease called *dystonia muscularis deformans*. He was aged about seven years when he was first treated. At first the movements were mainly unilateral and were stopped by the injection of alcohol in area 6; that kept him free for about four months. Later the area was destroyed with diathermy; that kept him under control for about two years, so that he learned to ride a bicycle and to typewrite and was able to go to school. At the time of the meeting the boy was aged about sixteen years; he was ambulatory, but not cured, and he had had fits. Dr. Money said that that was what frightened him. Was interference with the cortex going to turn the patient into someone who had fits? Another procedure for the relief of Parkinsonism had been advocated by Tracy Putnam. Dr. Money had seen one man, aged about seventy years, who had been operated on about ten days earlier by section of the lateral cortico-spinal tract in the second cervical segment of the cord. The operation was performed on one side only, but the tremor had stopped and the patient was beginning to move the arm and leg. The other side was to be treated later. Dr. Money was inclined to think that that operation might be worth while for patients with severe unilateral tremor and rigidity. It was a dangerous area with which to interfere, but although proper care was required, it was not more than that required with the cortical operation, which carried the danger of metabolic disturbance. Dr. Money thought that the post-operative coma-like state mentioned by Dr. Reid might be due to stasis in the longitudinal sinus and the veins draining into it from the cortex of the frontal lobes, which might be put out of action for a time. He had seen the condition follow other operations. The work on the surgical aspects of Parkinsonism was very interesting; Dr. Money hoped that Dr. Reid would go on with it and that he might be able to evolve other procedures which would be more satisfactory.

DR. WILLIAM C. GIBSON said that it was only fitting that in Sydney, where A. W. Campbell had worked for so long, they should have someone attempting to deal with the cortex in the most difficult of all diseases of the nervous system to treat surgically when it might well be of medical origin. Dr. Gibson said that he had been getting statistics about the increasing longevity of the population in Australia. The people graduating in medicine now would see in their lifetime a doubling of the population aged over sixty-five years in Australia. The question was whether that would mean a doubling of the number of cases of Parkinsonism. Although it was not necessarily a disease of old age, it was one of the problems of an aging population. One of the most fruitful approaches would be the cutting of the internal capsule. Jefferson Browder had presented his results in Montreal over a year earlier on sectioning the internal capsule which gave a man a limp arm but relieved him of his tremor. Dr. Gibson said that he had much praise for Dr. Reid's courage in plunging into this stream. Klemme and a section of the non-medical Press had done much to put the operation beyond the reach of right-thinking surgeons for years to come. With regard to the selection of patients for operation, Dr. Gibson said that it was right to concentrate on the older patients for whom nothing else could be done; by so doing they would learn much about cortical physiology. Dr. Gibson discounted the danger of epilepsy in the later age group; he said that was no contraindication. The operation should not be lauded as a cure-all that could be performed on the earlier age group. There was yet another approach in treatment, by the use of a drug, "Myanesin", which was supposed to act on the basal ganglia. It could be used intravenously only at the present time and had a sclerosing effect. But it might be one of the forerunners of drug treatment. If a number of clinics interested in the disease would investigate the use of that or a similar drug in a series of cases, some progress might be made. Dr. Gibson said that he was glad to have heard Dr. Reid give an account of his work. A neurological home was needed in Sydney; many men were

interested in the neurological sciences, but they lacked a central place in which to work.

Colonel McIntosh, from the chair, said that a mere outsider hesitated to express any opinion about work of the nature under discussion; but it did seem that the various procedures suggested indicated that the attack on the problem was still in the experimental stage. Surely Dr. Reid's results justified his proceeding along the lines which he had adopted, with a view to achieving better results still with increasing experience. It was heartening to hear of a non-surgical approach to the treatment of Parkinson's disease, which was so disabling and so inexorable in its progress, and the final results of which were so embarrassing to the patients themselves and to all associated with them.

Medical Societies.

MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held on May 12, 1948, at the Children's Hospital, Carlton, Melbourne, the President, DR. MOSTYN POWELL, in the chair.

Torsion of Abdominal Viscera.

DR. MURRAY CLARKE showed three patients with torsion of abdominal viscera which simulated acute appendicitis. He pointed out that in each case the five cardinal features of appendicitis were present—abdominal pain, tenderness, rigidity, vomiting and fever—and that in the presence of these features and in the absence of another diagnosis, operation should never be delayed.

Torsion of Caecum and Ascending Colon.

Dr. Clarke's first patient was a girl, aged thirteen years, who had complained of central abdominal pain and vomiting for two days and had eaten very little during that time. Her bowels had not been opened for two days. Her temperature was 99·6° F. and her pulse rate was 100 per minute. The tongue was coated and the breath offensive. The abdomen moved with respiration and was tender generally, although the maximum tenderness was in the left iliac fossa. Definite rigidity was present in the left iliac fossa with some fullness, but no mass was palpable. Rectal examination revealed an empty rectum with no tenderness or palpable mass. The abdomen was opened through a right paramedian incision, because it was thought that there was an inflamed appendix pointing over to the left side, or a transposition of viscera. A considerable amount of clear fluid was present and a purplish mass was found incarcerated in the pelvis on the left side with tæniæ stretching over it as tight bands. Because of fear of rupturing some gangrenous distal part, the mass was first aspirated through a purse-string suture with a hypodermic syringe and much gas was drawn off. The mass was then clearly found to be caecum and ascending colon on a very long mesentery. When the volvulus was untwisted through 240° its anatomical relations were clearly defined. The transverse, descending and sigmoid colon appeared normal, but the caecum was œdematous, very heavy, enormous in size and full of soft fæces. The caecum was then anchored to the anterior abdominal wall. Convalescence was uneventful.

Commenting on the case, Dr. Clarke said that volvulus of the caecum was rare, Miller (1940) finding one case in 136 of intestinal obstruction at the Mayo Clinic. It depended for its production on an excessive downward prolongation of the caecum and ascending colon and also failure of the normal fixation of the colon during the twelfth week of intrauterine life. Clockwise rotation was not surprising as the caecum rolled towards the centre of the abdomen (Kustner's law). It was more commonly associated with volvulus of the small intestine in which there was a universal mesentery common to large and small bowel and able to rotate freely about the axis of the superior mesenteric artery. Usually there was an onset of sudden intense abdominal pain and vomiting, and a localized tympanitic mass was often found in the left hypochondrium. Early operation was essential because of the 80% mortality. The caecum and ascending colon might be anchored to the "paracolic" gutter after Waugh's technique or the caecum might be anchored to the operation incision.

Torsion of Ovary containing Simple Cyst.

Dr. Clarke's second patient was a girl, aged six years, who, four days prior to admission to hospital, had been stricken suddenly with abdominal pain and had vomited several times and had still had pain. For the past twenty-four hours there had been no vomiting but persisting pain. She had a flushed face and anxious expression and was very dehydrated. Her temperature was 100·4° F., her pulse rate 100 per minute and her respiration rate 28 per minute. Her tongue was coated slightly. Generalized abdominal rigidity and tenderness of a pronounced degree were present. Shifting dulness was elicited. No rectal examination was made. She was regarded as a very sick subject of appendicitis with generalized peritonitis, and intravenous administration of glucose and saline solution was commenced before operation. Much heavily blood-stained fluid escaped when the abdomen was opened and a black tumour was seen and felt in the pelvis. When delivered it was found to be a grossly engorged left ovary and Fallopian tube which was twisted through 360° close to the body of the uterus. This gangrenous portion was removed and convalescence was uneventful. Examination of a microscopic section carried out by Dr. Reginald Webster showed an ovarian mass containing a thin-walled cyst lined by cuboidal epithelium; all other tissue was disorganized by interstitial hæmorrhage.

Torsion of Ovary containing a Dermoid Cyst.

Dr. Clarke's third patient was a girl, aged ten years, who had, two days previously, complained of pain in the left upper quadrant of the abdomen and had vomited several times. Twenty-four hours later the pain had moved to the right upper quadrant and she was still vomiting occasionally. The symptoms then subsided but returned twelve hours later when the pulse rate rose and she was considered to have acute appendicitis with generalized tenderness and rigidity. Her bowels had not been opened for two days and she had frequency and scalding of micturition for twenty-four hours. Her temperature was 99·2° F. and her pulse rate 98 per minute. A McBurney's incision revealed free blood-stained fluid and a mass in the pelvis. A right paramedian incision was then made and a gangrenous mass three inches in diameter was found in the pelvis. The wounds were closed and the patient brought to the Melbourne Children's Hospital—a journey of four hours' duration. She arrived in good condition, and after a little resuscitation the paramedian incision was reopened and the black mass—a large ovarian cyst (containing blood clot, hair and fatty sebaceous material) and the left Fallopian tube twisted in an anti-clockwise direction and gangrenous as far as the cornu of the uterus—was delivered and removed.

Commenting on this case, Dr. Clarke said that Sir John Fraser had stated that ovarian tumours were so infrequent in childhood that they might be disregarded in differential diagnosis. Smith and Butler in 1921 reviewed all the literature up to that date and found that only twenty-five instances of torsion of ovarian tumours before puberty had been reported and of those one-third had been diagnosed as acute appendicitis. Neither of the patients described by Dr. Clarke had reached puberty. He said that ovaries which developed torsion were usually abnormal. The types of tumours and cysts formed could roughly be classified as 60% malignant, 20% dermoid and 20% simple cysts. The usual symptomatology was low abdominal pain and vomiting. On examination there was no true abdominal rigidity and a mass was palpable rectally. Immediate operation was desirable.

DR. H. DOUGLAS STEPHENS complimented Dr. Clarke on a series of rare and instructive cases. He had seen only a few ovarian tumours and they were mostly dermoids. He had never seen a malignant one. He recalled a six-year-old child suffering from constant enuresis, day and night. A movable mass could be felt in the abdomen. An ovarian cyst was removed at operation, after which the enuresis ceased. Dr. Stephens said that most patients with intestinal obstruction due to malrotation that he had seen had complete rotation of the bowel, both large and small bowel being suspended by mesentery. The children in such cases had signs of obstruction on several occasions before the final attack. Sometimes some of the features were very obscure. He recalled one case in which the symptoms were neurological. The baby appeared shocked and lumbar puncture was advised, but the cerebro-spinal fluid was normal. When the abdomen was opened, the intestines were a slate grey colour and the peritoneum was full of blood-stained fluid. The rotation was corrected, but the child ultimately succumbed.

DR. ROBERT SOUTHBY said that one point of interest he had observed in the history of the patients presented was that in the two cases of ovarian tumour the pain was referred to the upper part of the abdomen. That might be significant. Another point was the size of the tumours. They were the

size of three fists, and yet rectal examination did not disclose them. He wondered if light anæsthesia might not be revealing in such cases. The big girl with volvulus of the caecum raised another point. He recalled a similar case in which a number of attacks of abdominal pain were labelled cyclic vomiting. The child actually had a complete volvulus of the large bowel. Dr. Southby said he was always sceptical of so-called cyclic vomiting. Several conditions labelled as such proved to have a definite mechanical basis.

Dr. Clarke in reply thanked the speakers for their remarks. He regretted that he had not made clear the difference between the two types of incomplete congenital fusion of the mesentery. The type described by Dr. Stephens had a universal mesentery. There was volvulus not only of the caecum and ascending colon, but of the small intestine as well. Cases had been described in which fusion was not complete; only portion of the ascending colon might be affected as in that case. In reply to Dr. Southby, Dr. Clarke said that the pain was present in the upper part of the abdomen in only one case of ovarian cyst. Concerning the size of the tumour, Dr. Clarke said that had an examination been made under anæsthesia, it would easily have been felt; but the diagnosis was not made before the operation, and the combined rectal and abdominal examination was not used. Dr. Clarke said he would like to mention one other point in diagnosis, namely, the use of X-ray examination in cases of intestinal obstruction. That might show a large air-containing mass in the left iliac fossa or possibly more than one fluid level. It was the custom to carry out X-ray examination in some hospitals, a practice that might be adopted with benefit in abdominal catastrophes.

Coarctation of the Aorta with Subaortic Stenosis and Aortic Insufficiency.

Dr. Mostyn Powell said that in July, 1946, a male child, then aged twenty-two months, was admitted to the Children's Hospital with typical left basal pneumonia. Two other striking features were pronounced cyanosis and a harsh systolic bruit audible all over the precordium. The pneumonia rapidly resolved under penicillin and sulphonamide therapy and the cyanosis disappeared; the need for elucidation of the exact nature of the cardiac lesion remained. The heart appeared to be of normal size, a faint thrill was palpable over the upper art of the sternum, and the bruit was of moderate intensity, systolic in time and faintly audible posteriorly. The real clue was given by femoral palpation. There was no femoral pulse and no blood pressure reading was obtainable in the legs; there were equal readings in the two arms of 140 millimetres of mercury (systolic) and 80 millimetres (diastolic). X-ray examination showed a small aortic knob, a concave left upper cardiac border, and what appeared to be a somewhat large left ventricle. A diagnosis was made of coarctation of the aorta.

In October, 1947, he was readmitted because of recurrent epistaxes of severity sufficient to reduce the hæmoglobin value to 50% and the red cell count to 2,600,000 per cubic millimetre. His admission was again due to recurrent epistaxis, but he was otherwise symptomless, and opportunity had been taken to study the cardiac condition further. It was apparent that there was more present than an uncomplicated coarctation of the aorta. The heart appeared large, the apex beat being in the fifth intercostal space just outside the nipple line; there was a finger's breadth of right cardiac dulness; there was strong pulsation and a thrill over the upper part of the sternum but maximum above the inner end of the right clavicle and in the jugular notch. The original bruit was louder; it was maximum to the right of the manubrium and at the medial end of the supraclavicular fossa, where it was accompanied by a long diastolic bruit, so long in fact that the sounds in that region were strikingly suggestive of the machinery murmur of the patent *ductus arteriosus*. At the apex there was a faint early diastolic bruit. Screening showed rather large left and right ventricles, gross pulsation of the ascending aorta and a fairly clear aortic window in the left anterior oblique position. There was some enlargement to the right of the sternum, and the left upper border of the cardiac contour was markedly concave resembling the tetralogy contour. The blood pressure remained at 140 millimetres of mercury (systolic) and 80 millimetres (diastolic) in both arms. It was not obtainable by audible manometry in the legs; some movement of the mercury column was visible at a height of 110 millimetres. The femoral pulse was absent, but it had been possible to feel the pulsation of a smaller vessel in that region, conceivably an enlarged superficial epigastric artery acting as a collateral. Around the periphery of the right scapula it was possible to palpate a pulsating vessel indicating the early development of collaterals. The electrocardiogram was normal. Those findings altered the early view that the child had simple coarctation of the aorta. Actually they fitted in well with a condition described by Abbott in 1928 and recently by Taussig in which in addition to the coarctation there was subaortic stenosis and aortic insufficiency. The subaortic stenosis was caused by a band of fibrous tissue, thought to be the remains of the bulbar septum which separated the aortic and pulmonary trunks and which in the types of cases under discussion persisted about one centimetre below the aortic valves and caused stenosis. An X-ray picture from Dr. Taussig's book was projected onto the screen and its extraordinary similarity to that in the present case was noteworthy.

Dr. Powell said that in view of the excellent exercise tolerance of the boy (apart from his epistaxes he was symptomless) the coarctation appeared to be of the adult type. Apart from the aortic lesion it would be subject to four possibilities: (i) a long symptomless normal life; (ii) a hypertensive syndrome in the upper part of the body with headaches, vascular accidents *et cetera*, and vascular deficiency syndrome in the inferior extremity with intermittent claudication *et cetera;* (iii) subacute bacterial endocarditis; (iv) rupture of the aorta. It was rather early to predict the future of the child, but the presence of an aortic lesion certainly altered the prognosis. Successful correction of the coarctation could produce nothing but improvement; the presence of the combined lesion and the freedom from symptoms, however, conduced towards conservatism for the present, and observation and review over the next few years.

Dr. Lawrence Stokes said that there appeared to be no doubt about the coarctation. He had never seen the combined lesion described, but Dr. Powell's explanation and interpretation must be accepted. He advised that the patient be watched and reviewed from time to time. Perhaps operation might be carried out in two or three years' time.

Dr. Kate Campbell asked why there was evidence of right ventricular hypertrophy.

Dr. Robert Southby asked at what age evidence of a collateral circulation became evident. He agreed that surgery should not be considered at the present time.

Dr. Alan Penington said that in view of the fact that the coarctation was not uncomplicated, the question of surgical approach was altered. Surgery for coarctation of the aorta was not a light undertaking to embark upon. Was it not better to confine the operation to simple uncomplicated cases and to be chary of such cases as that, in which so much was unknown?

Dr. Pat Cody said that coldness and pain in the lower limbs might be expected as evidence of the insufficient blood supply to those parts.

Dr. Powell in reply said that there was some difference of opinion about the operation. The Baltimore school were reluctant to operate in cases of that type, but in Boston Gross had carried out twenty-three operations with two deaths, and strongly advocated it. In the particular instance under discussion the coarctation was complicated and a waiting policy was indicated. It was well known also that several men went through the first world war though suffering from the anomaly and a case in a man aged ninety years had been reported. So unless hypertensive symptoms developed or ulcerative endocarditis complicated the issue, surgery should not be considered. Dr. Powell said that the right ventricular hypertrophy must be regarded as a back-pressure effect; it was not seen in uncomplicated cases. The collateral circulation usually was apparent at puberty. Pain in the lower extremities of the intermittent claudication type did not usually occur at that age, but might occur later, especially if the coarctation was extreme.

(To be continued.)

Correspondence.

GROUPING OF STREPTCOCCI.

Sir: In a recent number of *The Lancet*, that of August 14, 1948, there appeared an account of a new method for the preparation of extracts of hæmolytic streptococci for Lancefield grouping. This method, which has been developed by Mr. W. R. Maxted, of the Central Public Laboratory at Colindale, London, involves the use of a proteolytic enzyme produced during growth of a special strain of streptomyces, and considerably simplifies the procedure of streptococcal grouping. It may therefore be of interest to readers of

your journal whose work entails the grouping of streptococci, to know that I have recently brought from London a culture of this streptomyces. I shall be glad to send a subculture of this organism to anyone who cares to write to me.

Yours, etc.,
PHYLLIS M. ROUNTREE.

Fairfax Institute of Pathology,
Royal Prince Alfred Hospital,
Camperdown, New South Wales.
October 14, 1948.

Post-Graduate Work.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

Week-End Course at Warrnambool.

THE Melbourne Permanent Post-Graduate Committee announces the following details of a week-end course to be held at Warrnambool Base Hospital on November 20-21, 1948.

Saturday, November 20: 2.30 p.m., Dr. E. E. Dunlop, "Some Advances in Gastric and Œsophageal Surgery"; 8 p.m., Dr. J. Frew, "Management of Thyreotoxicosis".

Sunday, November 21: 10 a.m., Dr. L. W. Gleadell, "Management of Backward Displacement of the Uterus"; 2 p.m., Dr. Mostyn L. Powell, "Pædiatric Experience Abroad".

The fee for the course is £2 2s. Dr. F. J. Hetherington, Warrnambool, will make enrolments and advise those interested regarding arrangements for dinner on Saturday and Sunday.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Seminar in Medical Statistics.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that Miss Helen Newton Turner will conduct a seminar entitled "Association between Observations which can be Classified but not Actually Measured" in the Maitland Lecture Theatre, Sydney Hospital, on Wednesday, November 10, 1948, at 5.45 p.m.

Obstetrics and Gynæcology.

Post-graduate residencies for short periods can be arranged at the Women's Hospital, Crown Street. Early application is essential and fees payable are £5 5s. per week. When accommodation for similar residencies is available at the Royal Hospital for Women, a further announcement will be made.

Week-End Course at Bega.

In conjunction with the Far South Coast and Tablelands Association, a week-end course will be held at the Bega Valley County Council rooms, Auckland Street, Bega, on Saturday and Sunday, November 13 and 14. The programme will be as follows.

Saturday, November 13: 2 p.m., welcome to visitors by chairman of association, Dr. L. Wing; 2.30 p.m., "Present Day Trends in Obstetrics", Dr. T. Dixon Hughes; 3.45 p.m., "Thyreotoxicosis", Dr. Selwyn G. Nelson; 4.45 p.m., discussion.

Sunday, November 14: 10 a.m., "Gynæcological Complications of Pregnancy and their Treatment", Dr. T. Dixon Hughes; 11.30 a.m., "Treatment of Cardiac Failure with Reference to Electrocardiograms", Dr. Selwyn G. Nelson.

Fee for attendance will be £2 2s. Those desirous of attending are requested to communicate with Dr. F. J. Ireland, Honorary Secretary, Far South Coast and Tablelands Association, Gipps Street, Bega, as soon as possible.

Programme for January, 1949.

Advanced Medicine.

A fifteen-weeks course in advanced medicine suitable for M.R.A.C.P. candidates will begin on January 3, 1949. The programme has been arranged to take place almost exclusively in the afternoons. Application to attend the whole or portion of this course should be in the hands of the Course Secretary, 131, Macquarie Street, Sydney, no later than December 17, 1948. Fee: £39 7s. 6d., or £2 12s. 6d. per week, payable at enrolment date.

Master of Surgery II.

A course of lectures and demonstrations suitable for candidates for part II examination of the degree of master of surgery of the University of Sydney will begin on January 10, 1949, for twelve weeks.

Gynæcology and Obstetrics II.

A twelve-weeks course for part II of the diploma in gynæcology and obstetrics will begin on January 10, 1949.

Laryngology and Otorhinology II.

A course for candidates for part II of the diploma in laryngology and otorhinology will begin on January 10, 1949, for twelve weeks.

Ophthalmology II.

A twelve-weeks course for part II of the diploma in ophthalmology will begin on January 10, 1949.

Fees for attendance at part II courses will be £31 10s., and early application, enclosing remittance, is essential. All inquiries should be addressed to the Course Secretary, the Post-Graduate Committee in Medicine, 131, Macquarie Street, Sydney. Telegraphic address: "Postgrad, Sydney." Telephones: B 6980-BW 7483.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Horne, Terence William, M.B., B.S., 1948 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
McEwen, Betty Jean Harvard, M.B., B.S., 1948 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Weaver, Judith, M.B., B.S., 1948 (Univ. Sydney), District Hospital, Bathurst, New South Wales.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Allison, Alexander Arnold, provisional registration, 1948 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Asher, Joan, provisional registration, 1948 (Univ. Sydney), Saint George Hospital, Kogarah.
Booth, Howard Keith, M.B., B.S., 1946 (Univ. Sydney), 354, Chapel Road, Bankstown.
Bulteau, Pamela, provisional registration, 1948 (Univ. Sydney), Base Hospital, Tamworth.
Burfitt-Williams, Thomas, provisional registration, 1948 (Univ. Sydney), Lewisham Hospital, Lewisham.
Christian, Verlie Olive, provisional registration, 1948 (Univ. Sydney), Lithgow District Hospital, Lithgow.
Dalgarno, Geoffery James, M.B., B.S., 1947 (Univ. Sydney), Flat 5, 198, Liverpool Road, Enfield.
Firkin, Caleb Lawry, M.B., B.S., 1947 (Univ. Sydney), Longworth Avenue, Wallsend, New South Wales.
Greenberg, Audrey, M.B., B.S., 1947 (Univ. Sydney), 10, Cross Street, Waverley.
Hartnett, Bruce Stevenson, provisional registration, 1948 (Univ. Sydney), Royal North Shore Hospital, Saint Leonards.
Harvey, Henry Peter Burnell, provisional registration, 1948 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Hearne, Edward Allen, M.B., B.S., 1947 (Univ. Sydney), Sydney Hospital, Sydney.
Laing, Mary Kathleen, provisional registration, 1948 (Univ. Sydney), Royal North Shore Hospital, Saint Leonards.
McGirr, Gwendoline Francis, M.B., B.S., 1943 (Univ. Sydney), 81, Rangers Avenue, Cremorne.
Melick, Roger Aziz, M.B., B.S., 1947 (Univ. Sydney), 43, Prince Street, Randwick.
Stepen, Henry Mitchell, M.B., B.S., 1947 (Univ. Sydney), 54, Barcom Street, Merrylands.
Aarons, Morris Vincent, M.B., B.S., 1947 (Univ. Sydney), 71, Staple Street, Kingsgrove.
Adams, Corona Mary Monk, M.B., B.S., 1946 (Univ. Sydney), 8, Kuring-gai Avenue, Turramurra.
Allison, Robert William, M.B., B.S., 1947 (Univ. Sydney), Marrickville District Hospital, Marrickville.

Arnold, Barbara Joan, M.B., B.S., 1947 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.
Backhouse, Juliet Nancy, M.B., B.S., 1947 (Univ. Sydney), 3, Hampton Flats, 2, Eaton Street, North Sydney.
Baker, Cecil Horace, M.B., B.S., 1947 (Univ. Sydney), 19, Shirley Road, Roseville.
Barnes, Lesley Helen, M.B., B.S., 1948 (Univ. Sydney), Sydney Hospital, Sydney.
Bear, Victor David, M.B., B.S., 1946 (Univ. Sydney), 108, Chandos Street, Haberfield.
Beveridge, John, M.B., B.S., 1947 (Univ. Sydney), 67, Milson Road, Cremorne.
Blackman, John Edward, M.B., B.S., 1946 (Univ. Sydney), 168, Woodland Street, Balgowlah.
Boden, Betty, M.B., B.S., 1947 (Univ. Sydney), Eastern Suburbs Hospital, York Road, Waverley.
Brandt, Donald Sutherland, M.B., B.S., 1939 (Univ. Sydney), 5, Vernon Street, Strathfield.
Brown, Alan Belfield, M.B., B.S., 1947 (Univ. Sydney), Western Suburbs Hospital, Croydon.
Brown, Shirley Le Vance, M.B., B.S., 1942 (Univ. Sydney), 33, Shirley Road, Wollstonecraft.
Budge, Alexander George Campbell, M.B., 1935 (Univ. Sydney), 15, Wentworth Street, Point Piper.
Byrne, Kevin Edward Geoffrey, M.B., B.S., 1947 (Univ. Sydney), "Lakemba Cottage", The Boulevarde, Lakemba.
Carmody, Francis Spohn, M.B., B.S., 1945 (Univ. Sydney), 3, Fisher's Avenue, Vaucluse.
Cary, Wilfred Hezlet, M.B., B.S., 1946 (Univ. Sydney), Kabadah, Cumnock.
Carne, Jeannette Constance, M.B., B.S., 1947 (Univ. Sydney), Sydney Hospital, Sydney.
Carroll, Brian Edward, M.B., B.S., 1944 (Univ. Sydney), Garfield Street, Riverstone.
Champion, Elizabeth Patterson, M.B., B.S., 1945 (Univ. Sydney), 33, Margaret Street, Manly.
Clarke, Arthur John Robert, M.B., B.S., 1947 (Univ. Sydney), Maitland Hospital, West Maitland.

Notice.

MUNITIONS SUPPLY LABORATORIES.

THE following information is published at the request of the general superintendent of the Defence Research Laboratories which come under the Commonwealth Department of Supply and Development.

The name of the Munitions Supply Laboratories has been changed to Defence Research Laboratories. This change of name has been made to emphasize the *raison d'être* of the establishment, which is to make laboratory investigations aimed at the development of new weapons and of methods of manufacturing military equipment, whether of new or conventional types. Because the development of secondary industries increases the defence potential of the nation, Defence Research Laboratories will continue, as it has done since the war, to provide technical service to private industry on the lines already defined.

Corrigenda.

IN the issue of the journal of September 25, 1948, at page 376 in the sixth line of the first column "28 millilitres" should read "2·8 millilitres". We regret that this error has occurred.

In the issue of the journal of October 9, 1948, in the account of Professor J. C. Spence's remarks made at the Perth Congress on "Appendicitis in Childhood", a typographical error has occurred on page 439, in the seventh line of the second paragraph in the second column. The figure "0·8%" should read "8·0%". We apologize to Professor Spence for this mistake.

DR. A. E. COATES has informed us that two mistakes have occurred in the reporting of his remarks made in the discussion on surgery of the gall-bladder and the common bile duct and on the making of abdominal incisions during the meeting of the Section of Surgery at the Perth Congress. On page 462, in the tenth line of the second column, "cholecystectomy" should read "cholecystostomy". On page 463, in line 53 of the second column, the sentence beginning "He offered one suggestion" should continue as follows: " . . . in an oblique incision in a fat patient, he stitched the skin edge back to the surrounding skin in order to convert the incision into a gaping hole." We regret these inaccuracies.

Diary for the Month.

Nov. 2.—New South Wales Branch, B.M.A.: Organization and Science Committee.
Nov. 3.—Victorian Branch, B.M.A.: Branch Meeting.
Nov. 3.—Western Australian Branch, B.M.A.: Council Meeting.
Nov. 4.—South Australian Branch, B.M.A.: Council Meeting.
Nov. 5.—Queensland Branch, B.M.A.: Branch Meeting.
Nov. 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
Nov. 11.—Victorian Branch, B.M.A.: Organization Subcommittee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute; Brisbane City Council (Medical Officer of Health). Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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